

Putting the Research Councils in their Place

ONE of the more pious of the British government's declarations in its white paper on research and development (see page 124) is that government departments should in future be more forthcoming with descriptions of their policies on research and development and explanations of how they have arrived at them. It is therefore not merely surprising but a little scandalous that the government itself has now arrived at some of the most important decisions on the administration of research to have been taken since the Second World War without substantiating these by argument and without even acknowledging that the many critics of Lord Rothschild's recipe for the reorganization of research had, at least, a case. The white paper is deviously innocent on, for example, the arithmetic which has presumably led it to conclude that £20 million a year might be transferred from the research councils to the government departments by the end of a transition period of three years. How precisely were these figures calculated? Which part of Lord Rothschild's list of projects that might be transferred from the Agricultural Research Council to the Ministry of Agriculture, Fisheries and Food have been scrapped so as to reduce the total transfer from £14.5 million to a mere £10 million? And what in any case does the government think of the objections made earlier this year to what appears now to be its policy which consisted of the assertion that as things are the research councils are much better equipped with good and perceptive people than are the departments which will, in future, become in part their masters? Although the government may have good reasons for believing that its present course is right, it is discourteous, to say the least, to have invited "wide public debate" and then to have shrunk from answering the points which have been raised. This is a miserable augury for the future as well as a likely exacerbation of the fury with which the new proposals will no doubt be greeted by the research councils, the universities and the scientific community as a whole.

It is also reprehensible that the government should have used the need for a response to Rothschild not only as a means of dealing with the administration of the research councils but as a means of announcing a reorganization of applied research in the government as a whole. From the beginning, it has been apparent that Lord Rothschild's inquiry should have begun not with the research councils but with the conduct of applied research supported by public money in the government as such. The research councils became a public issue merely because a government committee so secret that its existence was not disclosed officially to the Agricultural Research Council recommended that for practical purposes the ARC should be abolished. It is all very well for the government to say, now, that the affairs of the Ministry of Defence and of the Department of Trade and Industry are, in most respects, properly conducted according to the customer-contractor principle but it is a long time since

there has been an independent audit of this assertion. The Gibbs-Zuckerman report of 1962 was, after all, regarded at the time not as a definitive statement on the subject but rather as a set of objectives to which the government might aspire in its conduct of research and development. Since then, nothing of any importance has been done to test the efficiency with which these complacent customers deal with their contractors, and even though the Select Committee on Science and Technology has investigated some aspects of the areas of research and development in which the government spends the bulk of its money, its prejudices have clouded the value of the analyses it has made. So is it not ironical that there should now be a whole new framework for publicly supported research and development simply because the machinery for spending £20 million a year should have been called into question? The government's espousal of the doctrine of public accountability and open discussion would have been much more credible if it had shown that its own vested interests had been looked at carefully.

That said, what the scientific community must do now is to make the best of what the government has proposed. The white paper is sober, perceptive and intelligent. The past few months have seen far too much anxiety by the research councils about the working of the customer-contractor principle in their parish. There is no reason to fear that it will turn out to be either as harmful or as pernicious as the research councils have been saying. To be sure, the restrictions that may now be placed on the freedom to publish the results of applied research will be irksome, to say the least, and should be resisted. It is also unthinkable that the research councils should allow themselves to be put in the position of having to accept commissions for applied research without being provided with the resources with which to make the necessary fundamental investigations, which is why it is essential that means should now be found of regulating relationships between customers and contractors within the government machine in a manner reminiscent of the ways in which commercial customers and contractors do their business. The outcome could be beneficial for the research councils, but much will depend on the power of the new Council for Scientific Policy and on its independence. The central question is whether the unofficial members will have influence and whether they will have the wit not merely to give advice to Mrs Margaret Thatcher or her successor but to provide an effective stream of criticism of the way in which the government machinery for applied research is functioning. This is an issue which should be fought, and the Council for Scientific Policy could do worse than to begin by asking precisely what the government intends by its apparently nonsensical statement that the Department of Trade and Industry, in its administration of general applied research, should consist of two halves, one responsible for the interests of the customer and the other for the interests of the con-



tractors. In the long run, however, if the council plays its cards correctly, it could become an instrument for doing what the government has failed to do in the past few months—to provide a framework for making sure not merely that the research councils are a little more efficient but that public expenditure on applied science as a whole brings respectable returns.

Paying for Telephones

How is the British Post Office to finance its current modernization programme, and what is to be done, in the 1980s, when the Post Office will be (with a little luck) ready to spend money on the new microwave trunk network on which it has set its sights? In the past few days, the notion that private capital might be invited to contribute to the expansion programme has popped up again, and has no doubt brought joy to those Conservatives who consider that pound notes are distinguishable from each other by the test of whether they come from public or private sources—and who consider that the latter are more estimable. In reality, it seems unlikely that the government will seek to add this hot potato to its present host of problems, and the notion that private capital might be used to finance the development of telecommunications in Britain seems to have been given fresh life simply because of the reputation earned at the Department of Trade and Industry by Sir John Eden, the new Minister of Posts and Telecommunications, and by his sensible decision to equip himself with a financial adviser from the City, Mr Robin Hutton of Hambros Bank. Wherever the money comes from, however, there is no doubt that the financing of the Post Office's plans for capital expenditure will become—and should become—an important public issue in the months ahead.

Two facts stand out. One is that the Post Office is making an enormous demand on the public purse to make up for the under-investment of the 1940s and 1950s which left the telephone system in its present sorry state. The corporation is spending £2,700 million between 1970 and 1975 on capital equipment, ninety per cent of it on telecommunications. On present plans, this is no less than a third of all capital expenditure by nationalized industries in Britain. Half that sum must be found from the Post Office's own earnings and the other half borrowed from the Treasury. The second conspicuous fact is that even £500 million a year is not enough. There are still fewer telephones in all of Britain than in New York City alone, and the telephone waiting list is growing rather than shrinking as new telephones are installed at the rate of about 600,000 a year.

The more important question is whether the Post Office could efficiently and intelligently spend more money if it could lay its hands on it. The current expansion programme has already ruined the export performance of the British telecommunications industry. The industry (by which is meant chiefly the General Electric Company, Plessey Ltd and Standard Telephones and Cables Ltd) has trebled its deliveries to the Post Office since 1964 when there was a sudden awakening to the disastrous state of the telephones. Last year the industry delivered £220 million worth of supplies to the Post Office and exported only £44 million worth. (This figure, however, was

up 25 per cent over the preceding year and was accompanied by deliveries worth £32 million for other domestic customers in Britain.) But in the 1960s, both because of Post Office expansion and because the Post Office still demands that the bulk of its exchange equipment should be the old-fashioned Strowger step-by-step, the British telecommunications industry lost its export lead to West Germany and Sweden. Compare the British performance with that of L. M. Ericsson, Sweden's big telecommunications manufacturer, which last year sold 23 per cent of its products worth \$781 million to the Swedish telecommunications authority and exported the rest. Sweden is a small, well-developed country, of course, whose industries, more than those in Britain, depend on exports, but L. M. Ericsson's exports of switching equipment were the more sophisticated cross-bar type, and while continuing to expand their share of the Latin American market, they made even greater progress in Europe, where their sales increased 30 per cent over those of 1970. There is no market in Europe for British-made Strowger, which accounts for the bulk of British telecommunications exports.

The prospect is not much more hopeful for the decade ahead. Much of the new money which the Post Office plans to spend may go on the newly developed TXE-4 telephone exchange, a semi-electronic device with 10,000 lines and switches based on reed relays which is intended to bridge the gap between the old Strowger equipment and the solid state exchanges which must surely come into use in the 1990s. By all accounts, the Post Office is planning to decide on the installation of the TXE-4 by the end of 1972, and it could be right in thinking that this may be the best way ahead for the British telephone system as it stands. One difficulty is that countries abroad are not lumbered with as much Strowger equipment as Britain, and thus have less need for a new and expensive telephone exchange whose chief virtue is that it can harmonize with the old and the new. So far as the British telecommunications industry is concerned, even the investment in production facilities for the TXE-4 may not be profitable. It might be better if the Post Office were to buy Strowger equipment from abroad and to allow its domestic industry to produce the more sophisticated equipment that will be of immediate use to foreign purchasers, and which will be acceptable in Britain in the 1980s. Unhappily, however, there is no sign that the Post Office has yet accepted the good advice given it in 1968 by the Brookings Institution's report on Britain's economic prospects:

"It would be a serious mistake to induce a major enlargement of domestic capacity to produce conventional equipment, since the net yearly demand for this equipment will probably decline in the later 1970s. If the suppliers expand optimally for their own long-run growth, they would fall short of Post Office requirements for the next ten years. If instead they expand rapidly enough to meet Post Office needs, they will forgo chances to develop more advanced products as well as create seriously excessive capacity in narrow and obsolescent product lines."*

Nobody should underestimate the difficulty in which the Post Office finds itself. Large though the present scale of capital investment may appear, the growth in the first half of the 1970s is estimated to amount to merely

25 per cent—not very much for an enterprise whose business is growing at more than 10 per cent a year. Given that inflation continues apace, the Post Office might consider increasing the amount of money re-invested each year from its own resources. Technically, the Post Office must live with uncertainty about its dreams for the 1980s. Will it then be possible to embark without much hesitation on the conversion of the present system to one based exclusively on digital transmission, and will the microwave trunk network then be as attractive as it now promises to be? If the Post Office were a truly commercially minded organization, it would do everything it could to remove this uncertainty, which argues for a further acceleration of the research and development programme. There might even be a case for deciding that Britain might stagger on with a less good system of telecommunications than it needs for the remainder of this decade for the sake of faster progress in the 1980s. But whatever strategic decisions of this kind may be made, there is no doubt that the planning of telecommunications in Britain should be much more closely coordinated than seems at present likely with what is happening on the mainland.

* Britain's Economic Prospects. By Richard E. Caves and Associates. The Brookings Institution, 1968.

Roads and Planning

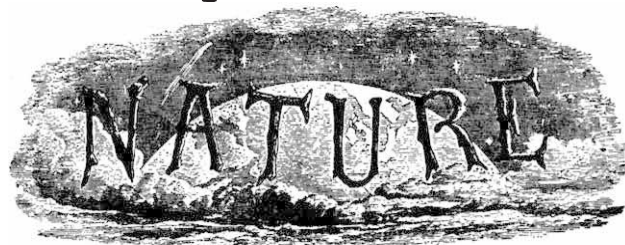
THE Greater London Council has predictably provoked the wrath of motoring organizations in Britain by issuing last week a discussion paper, *Traffic and the Environment*, which floats, among other suggestions, the possibility that off-street parking places might be taxed at a rate of between £150 and £250 a year. And, of course, it is a curious phenomenon to see how the GLC has now stood on its head its old policy on parking. A decade ago, nobody could build an office block in central London without providing a certain amount of off-street parking. Now the GLC insists that each new office building may not be provided with more than a certain amount of parking and plainly it is dickering with still more draconian measures, including the taxation of off-street parking and the requirement of supplementary licences for those who would bring vehicles into central London. The old objective of forcing parked cars off the streets has given way to the notion that moving vehicles should also be restricted. In present circumstances, and especially because the plans for building an inner ring of motorway connexions have now been lost in the fog of the public inquiry on the motorway box, there is much to be said for giving the council's proposals a serious hearing.

So far, so good. There is, however, an important sense in which the council's proposals are too narrow and too negative. It is all very well to promise that public transport will be improved, but everybody knows how long it takes to build a new underground railway, and there is at present no prospect that the underground network with which London is already equipped will be modernized (as it should be) in the foreseeable future. Worse still, however, the council seems to have been able to divorce the immediate problem of traffic congestion from the long-term question of how London as a whole should be planned. Moreover, the past few years

have seen far too casual and insensitive a replacement of older parts of the city by meretricious buildings, sometimes tawdry, sometimes pretentious (like the unfortunate building south of St James's Park which Sir Basil Spence has been allowed to design, no doubt on the strength of his good connexions and his Order of Merit).

The most immediate need is for a moratorium on the tasteless renewal of central London now well under way. Old buildings of no particular architectural merit may often be, by their familiarity and their associations, important parts of the fabric of the city. If the planning authority is willing to impose a levy on off-street parking spaces, should it not also impose a much greater levy on those who wish to knock down old buildings in those parts of the city where some of the old character survives? The GLC should also set out more energetically than it has done so far to reverse the drift of ordinary people from central London to the increasingly distant suburbs—itsself one of the potent generators of traffic. And for the more distant future, the planning authority should clarify in its mind a more modern concept of what a modern city should be like. The essence of any city is that those who live and work in it should be able to communicate with each other easily, not merely by telephone but face to face. In the days of the cart and the hansom cab, this could be done only if people were living cheek by jowl. But now there is no reason why some of the small towns thirty miles or more from central London should not be made integral parts of London by the provision of fast surface communications. The objective should be a cellular city with as much of present London as possible at the centre and plenty of what is called environment in between the cells.

100 Years Ago



DR. E. DECAISNE, in a note communicated to the Academy of Sciences on the 3rd of June, shows that from the triple point of view of the fecundity of marriages, of the absolute number of births, and of the excess of births over deaths, France occupies the lowest place of all the European States. In Prussia 100 marriages give 460 children; in France the same number of marriages give only 300 children. In Prussia the number of births for each 100 of the population generally is 3.95 per annum; in France there are only 2.55. In Prussia the excess of births over deaths in each million of the population is 13,000 per annum, whilst in France it only amounts to 2,400. "If we admit," says Dr. Decaisne, "as a conclusion from the above figures, that the doubling of the population of France, despoiled of two of its finest provinces, and by unheard of disasters, will require 170 years to be effected, whilst that of Prussia requires only 42 years, Great Britain 52, and Russia 66, some estimate may be made of the amount of the evil that has befallen this country." He does not hesitate to say that, as the first step towards the restoration of the former power of France, the first thing that should occupy her statesmen is the reconstitution, the reorganisation of human life; and everyone should throw aside that false patriotism which has been the cause of so much ill.

From *Nature*, 6, 250, July 25, 1872.

OLD WORLD

No Deal

THE Monopolies Commission took both the Department of Trade and Industry and the City by surprise last week with its verdict that Glaxo, Boots and Beecham must continue on their separate ways.

After five months of deliberation, the commission's verdict is simply that the mergers would damage the industry's research and development. It concedes that the mergers would have benefited research and development—rising costs are more easily met by big companies, research duplication is prevented and riskier projects might be tackled—but concludes that "the risks outweigh the gains". The mergers would remove the incentive for both Boots and Beecham to broaden the scope of their research, would eliminate one important (Beecham) or one potentially important (Boots) centre for deciding how research money should be spent, and, in the case of Beecham's bid, would damage the morale of Glaxo's research staff.

The commission's decision is based on its conviction that there is no relationship between size and success in research and development. Annual expenditure on pharmaceutical research and development by the three companies is £0.768 million (Boots), £6 million (Beecham) and £5.6 million (Glaxo) with Beecham and Glaxo rated 16th and 27th respectively in the world league of pharmaceutical companies. The proposed merger would have put a Beecham-Glaxo combine into the top ten and given a Boots-Glaxo combine a wider area of research than either company has on its own. But the commission holds that what evidence there is suggests that the increase in size would not necessarily produce an increase in success.

Accordingly the commission's chief grounds for rejecting the merger, the heart of its 107-page report is therefore a short appendix which discusses the problems of success in research and development and company size. Its conclusion is that research and development improves with company size up to a certain limit and then falls off, the threshold being annual sales of £150 to £180 million (Boots sales £257 million, Beecham's £181 million and Glaxo's £173 million in 1970-71). To confirm its findings, the commission ran two limited exercises (the details of which are not published in the report) and decided that the results backed by academic studies "although not conclusive in themselves" support the theory that size does not matter when it comes to

success in research and development; this is in spite of the fact that the NEDO report on the industry due for publication this September, which the commission studied, is reported to come to the opposite conclusion.

Essentially Beecham wanted Glaxo to create a more powerful marketing force, to provide more money for research and development and to broaden its somewhat limited pharmaceutical research. (The patents on Beecham's highly successful semi-synthetic penicillin, ampicillin, expire in 1975.) Boots held that the merger would enlarge its share of the international pharmaceutical market (its activities are chiefly home based, Glaxo's chiefly overseas) and strengthen the base of the two companies' research. Its own successful research department (producing Brufen, a drug for treating rheumatism and Furamide for treating dysentery) would, Boots claimed, ensure that the flow of information would not be all one way; the lack of overlap between the two companies' research should ensure that Glaxo's research effort would not be diverted or damaged by the merger.

The commission concludes however that competition is likely to stimulate more and better research than sheer size. Boots and Beecham, it argues, will expand their research anyway and the merger would simply remove the incentive for them to do so.

NRDC

Pollution Control

IN spite of increasing public concern with the environment during the past year there has not been a corresponding increase in the number of environmentally oriented projects submitted to the NRDC for support.

Two of the projects which the NRDC decided to support in this field in the past year were associated with the re-utilization of wastes whereas the remainder were projects designed to reduce pollution by better treatment of effluents. (*Environmental Pollution and Control; NRDC Interests and Activities*, I. C. Schomburgk *et al.*, NRDC, 1972.)

One of the re-utilization projects, a joint submission by an industrial chemistry group and Brunel University, is designed to recover useful materials by low temperature partial pyrolysis, whereas the other, which comes solely from industry, is designed to recover X-ray film.

The projects designed to treat effluent, for which the NRDC has budgeted £50,000, come, with one exception, from industry. Not surprisingly in view of public outcry during the past year, one of the projects is the development of a simple packaged plant to destroy

solid cyanide waste. The NRDC has also agreed to licence an electrochemical cell jointly for the University of Salford and an industrial group. The cell will oxidize phenols, cyanides and tar by-products, thus easing their disposal.

The NRDC took on eight projects in the past twelve months designed to improve the disposal of farm waste. These are all jointly financed by the corporation and industry and involve separation of liquid and solid waste, biological treatment processes and the development of package units to produce high quality effluent.

The NRDC is also supporting guarantee clauses related to performance on contracts for a high rate biological filtration medium which has been developed by an industrial group. The novelty of this development is the packing within the filter.

All these projects, according to a spokesman for the NRDC, come from smaller companies. The large companies, said the spokesman, are in general waiting on the sidelines to see which way the environmental wind is blowing before they invest money in pollution control.

RIVER POLLUTION

Cash for Clean Rivers

THE government is prepared to spend more than £600 million between now and 1980 to clean up Britain's rivers, according to Mr Eldon Griffiths, Under-Secretary of State at the Department of the Environment. Quoting from advance extracts from Volume II of the 1970 River Pollution Survey which deals with sewage and effluent discharges, Mr Griffiths revealed last week at Birmingham that 37 per cent of the number of sewage discharges are unsatisfactory by the river authorities standards. These amount to 60 per cent of the total volume of sewage effluent discharged. Almost all crude sewage discharges, however, are considered unsatisfactory.

The chief cause of these frightening statistics, according to the survey, is overloading, which can only be relieved by additional and improved plant. To bring all sewage and effluent discharges up to the standards that river authorities expect to impose by 1980 will cost £610 million (1970 prices), or about £12 per head of the population. These figures do not include expenditure on sewage piping or on the replacement of worn-out equipment which could amount to a further £600 million.

The survey also reveals that rivers and canals receive about 4,000 million gallons of sewage effluent, crude sewage, industrial effluent and mine water a day. Sixty-four per cent entered non-tidal

waters, thirty-five per cent tidal waters and only one per cent canals. The total represents about 83 gallons of liquid waste per day for each person in England and Wales. In addition nearly 15,000 million gallons of industrial cooling water are discharged into rivers and canals daily.

If £1,200 million is spent by 1980, eighty per cent of non-tidal rivers should be free from pollution, fifteen per cent will be mildly polluted, three per cent badly polluted and one per cent (199 miles, as compared with 952 miles in 1970) grossly polluted. Tidal rivers would still be in a rather worse state, with three per cent grossly polluted, twelve per cent badly polluted, twenty-eight per cent mildly polluted and only fifty-six per cent free from pollution.

In spite of the long term nature of this programme, progress has already been encouraging. In the eighteen months since the survey, Mr Griffiths said, 362 miles of previously polluted rivers have become pollution free.

The full version of Volume II should be available in a few months time, and the government hopes to put its Water Reorganization Bill before Parliament in the next session.

SPACE

America Will Wait

THE United States is now prepared to wait until the autumn for Europe to decide what part it wants to play in the post-Apollo programme. Dr Edward E. David, President Nixon's science adviser, indicated as much last week, stating that the United States hoped the problem would be resolved by the autumn and that the project can then proceed. This postponement (Europe's original deadline was this month) follows the cancellation of last week's European Space Conference which was to decide Europe's attitude to the shuttle.

Dr David, who was in London following a visit to the USSR to follow up President Nixon's agreements on scientific and technological cooperation, also tried to calm British fears that participation in the shuttle will be an expensive waste of time. Originally, Europe hoped that the 10 per cent involvement (about \$650 million) that the Americans were suggesting would mean that Europe would develop the space tug. It appears now that NASA plans to let Europe have nothing more exciting than the development of the research applications module (RAM). Mr Edward Heath, the Prime Minister, said in the House of Commons on July 4 that Europe's participation is now limited to "normal technology". Dr David said, however, that he thought RAM a highly attractive proposition. It is

also attractive economically, Dr David said, as it is the only large production item in the shuttle programme; as many as 50 RAMs might in fact be needed.

Dr David also renewed American assurances that NASA's launch facilities will be available to Europe on an "open basis"—the only riders being that the United States must obey international

law and honour its commitments to international organizations. He did concede, however, that American science and space policy—including the shuttle—could change if a new administration was elected in November; "however, I personally have no doubt that it's going to go forward in essentially the way it is now".

Recovery by Fischer

Although it might appear that most of the excitement in the Spassky-Fischer match seems to have occurred off the board rather than on it, the actual play, so far, has certainly disappointed the large entourage of followers.

The first game opened quietly with a variation of the Nimzo-Indian defence (by transposition), remarkable only by the fact that Fischer has rarely used this defence. Spassky was probably caught off guard a little by this and was able to set his opponent only minor problems to solve. Fischer defended well until his fateful 29th move when he chose a risky sacrifice of a bishop for two pawns in the endgame. This sacrifice proved to be unsound but it required accurate play by Spassky to capitalize on this, particularly to avoid the stalemate trap that Fischer must have been hoping for.

The second game was unaccountably defaulted by Fischer, an occurrence which is unprecedented in the history of world championship matches. It would be tragic for Fischer if this point loss turned out to be decisive.

The third game with Spassky playing with the white pieces again was played in a very fine way by Fischer. His opening play was original and

aggressive (especially his 11th move), and Spassky appeared to be placed off guard a second time. He allowed Fischer to obtain the superior position by virtue of the advantage of the two bishops, a weak white king's pawn, and a mobile "queen's side majority" of pawns. The crisis of the game probably arose at the 31st move when Fischer must have realized that in order to make progress he would have to relinquish one of his powerful bishops, win the king's pawn and force an entry into Spassky's position. The presence of opposite coloured bishops could give hopes of a draw for Spassky, but Fischer avoided the exchange of queens and demonstrated that the position of the white king was too weak to resist the ensuing attack.

J.P.

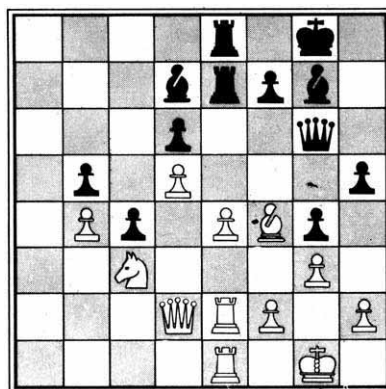
THE THIRD GAME

White : Spassky, Black : Fischer
Benoni

WHITE	BLACK
1 P-Q4	N-KB3
2 P-QB4	P-K3
3 N-KB3	P-B4
4 P-Q5	PxP
5 PxP	P-Q3
6 N-B3	P-KN3
7 N-Q2	QN-Q2
8 P-K4	B-N2
9 B-K2	O-O
10 O-O	R-K1
11 Q-B2	N-R4
12 BxN	PxB
13 N-B4	N-K4
14 N-K3	Q-KR5
15 B-Q2	N-KN5
16 NxN	PxN
17 B-B4	Q-B3
18 P-KN3	B-Q2
19 P-QR4	P-N3
20 KR-K1	P-QR3
21 R-K2	P-N4
22 QR-K1	Q-N3
23 P-N3	R-K2
24 Q-Q3	R-N1
25 PxP	PxP
26 P-N4	P-B5
27 Q-Q2	QR-K1
28 R-K3	P-R4
29 R3-K2	K-R2
30 R-K3	K-N1
31 R3-K2	BxN
32 QxB	RxP
33 RxR	RxR
34 RxR	QxR
35 B-R6	Q-N3
36 B-B1	Q-N8
37 K-B1	B-B4
38 K-K2	Q-K5ch
39 Q-K3	Q-B7ch
40 Q-Q2	Q-N6
41 Q-Q4	B-Q6ch
Resigns	

FISCHER

BLACK



WHITE

SPASSKY

Position in the third match game after
White's 31st move

The Rothschild Ship Comes Home

THE British government has for practical purposes accepted the chief recommendations of the Rothschild report on the administration of civil science and in particular the recommendation that a substantial part of the money at present spent by the research councils should be transferred to the parliamentary votes of what are called the customer departments. The government's proposals are spelled out laconically, and without more than an indirect reference to Lord Rothschild's "customer-contractor principle", in a white paper published this week (*Framework for Government Research and Development*, HMSO, £0.13). On the research councils, the government says that it intends to retain the present system under which the councils are responsible to the Secretary of State for Education and Science but it says (leaning on Sir Frederick Dainton's recipe for reform for justification) that government departments should in future be "more closely associated in framing the council's programmes". It goes on to say that departments will be provided with the funds needed to commission applied research in some of the areas covered by the research councils.

One practical consequence is that the Council for Scientific Policy, which at present advises the Secretary of State for Education and Science, will be reconstituted but it will still be a purely advisory body. The intention is that the executive head of each of the five research councils will be a member as of right of the reconstituted council, as will be the chairman of the University Grants Committee. Government departments interested in the work of the research councils will also be represented, as will the Chief Scientific Adviser to the government. There will also be independent members, one of whom will be chairman, but at this stage there is no way of knowing whether the independent members will be a majority or a minority.

As a token of the influence of the customer departments of government on the research councils, the government has agreed that future appointments to the research councils, although still formally the responsibility of the Secretary of State for Education and Science, will be made only with the agreement of other government ministers with an interest. Government departments will be represented on the research councils in future by full members and not, as at present, by assessors.

Three of the five research councils are affected by the proposals to transfer funds from the budgets of the research councils to the customer departments—the Agricultural Research Council

(ARC), the Medical Research Council (MRC) and the Natural Environment Research Council (NERC). The ARC has escaped a little more lightly than the Rothschild recipe would have required—the Rothschild document urged that £14.5 million of the £18.7 million allotted to the ARC in 1971–72 could be transferred to customer departments, principally the Ministry of Agriculture, Fisheries and Food, but the government's decision is that there should be a transfer of £10 million in 1975–76. For the research councils as a whole, the intention is that £10 million should be transferred to customer departments in the coming financial year, that £15 million should be transferred in 1974 and £20 million in the following financial year (see table 1). The government says that these estimates will be exceeded in the years ahead by the transfer of extra amounts of money proportional to the growth in the total science budget, which is expected to increase from £125 million in the current financial year to £140 million in 1974–75 (at 1971 prices).

Among the customer departments, the Ministry of Agriculture, Fisheries and Food will be the chief beneficiary, with £10.5 million to spend in 1975–76 out of a total transfer of £20 million. The Department of Health and Social Security will get £5 million and the Department of Trade and Industry £2.5 million. The government says that the reconstituted Council for Scientific Policy will be expected to make recommendations about the effect of the new system on the council, but that there should be a period of stability during the three coming financial years and no review until the transfer planned at present has been completed. The recommendations of the Council for Scientific Policy will be considered "in planning future totals of public expenditure on research and development".

The government has laid down a few of the rules that will regulate the spending of the sums of money to be transferred to customer departments. First, it says that no conditions will be placed on the use of this money but "the expectation is that it will be spent to commission applied research work from the research

councils". Departments will have to justify their expenditure on research work under this category, but will be allowed to spend some of the money on providing the research councils with capital facilities. It will be for departments to define the objectives of commissioned research, but councils will be free to refuse work, possibly on the grounds that projects are not scientifically feasible or that adequate resources are not available. The research councils will be responsible for the detailed management of commissioned research and although councils "may normally expect" to be free to publish the results of commissioned work, there may be circumstances when departments "must reserve their position on publication".

The Nature Conservancy will undergo a considerable metamorphosis if the government's proposals are adopted. The white paper says that the part of the conservancy's programme concerned with the management of the environment would be best funded as part of an environmental programme, but that the research work which is carried out is more appropriate to the general programme of the Natural Environment Research Council. As a result, the government says, there have arisen "stresses difficult to resolve within the present framework" and that the time has come "to make a fresh start". For this reason, it says that present expenditure on the management of nature reserves (£1.1 million in 1971–72) together with about £0.3 million for commissioning applied research will be transferred to the general budget of the Department of Education and Science in April 1973. The Nature Conservancy Committee of the Natural Environment Research Council is to be abolished, and a new Nature Conservancy Council will be established to manage the nature reserves. But the laboratories and staff of the Nature Conservancy as it is at present will remain with the Natural Environment Research Council.

In much the same spirit, the government has decided that the Soil Survey of England and Wales will continue to be run by NERC but that the funds will be transferred to the Ministry of Agriculture, Fisheries and Food from April 1973. The Institute of Hydrology, in recent months regarded as one of the potential victims of the government's white paper, will remain with NERC

Table 1. Proposed Transfers to Customer Departments

	Present budget	Rothschild recipe	(£M at 1971–72 prices)		
			Government proposals		
			1973–74	1974–75	1975–76
ARC	18.7	14.5	5.0	7.5	10.0
MRC	22.4	5.6	2.75	4.25	5.5
NERC	15.3	7.6	2.25	3.25	4.5
	56.4	27.7	10.0	15.0	20.0

but the white paper says that a final decision will be taken only when future arrangements for the management of water resources in Britain have been worked out.

The Science Research Council and the Social Science Research Council are for the time being immune from change, largely on the grounds that they are principally occupied with university research and the support of postgraduate students. The government says that there may in future be a demand for commissioned research placed by government departments with the SSRC, but that this will be "new and additional work". On the Science Research Council, the white paper says that a study is being made of the ways in which there may be an overlap between its activities and those of the Department of Trade and Industry and the Department of the Environment.

One of the recommendations of the Rothschild report, and a central issue in the public discussions of the past few months, has been the question of whether government departments in Britain are at present equipped, with people of the right calibre, intelligently to commission applied research from the research councils. The government now says that it will in future hold ministers responsible for seeing that departmental objectives are properly backed by research and development. It says that departments must define their requirements "in the clearest possible terms" and that there must be a partnership between departmental customers and research and development contractors so that responsibilities are clear. The white paper says that the government reaffirms its intention, announced in its preface to Lord Rothschild's recipe, of extending this principle to all publicly supported research and development. The government is more cautious about Lord Rothschild's proposal that there should be a general research surcharge of ten per cent on commissioned applied research so as to allow the research and development contractors, at least when they are research councils, to pursue more fundamental lines of enquiry. The white paper says that the government accepts the proposal in principle but that there are circumstances in which the provision will have to be varied.

In passing, the white paper says that it cannot accept the notion, dear to the heart of the Select Committee on Science and Technology, that there should be a Minister for Research and Development. Applied research and development, the white paper says, are a necessary part of government and cannot be separated from the responsibilities of ministers. But the Chief Scientific Adviser to the government

should in future be responsible for advice on the way in which the new arrangements for the management of applied research are functioning and he has also been asked to suggest how government departments should in future make more information about research and development programmes publicly available.

In a review of how government departments are at present equipped to handle applied research, the government says that the Ministry of Defence already spends £330 million a year, most of which is at present regulated by the customer-contractor principle. The Department of Trade and Industry's expenditure on civil aerospace (£109 million in the current financial year) is similarly said to be organized on customer-contractor lines. The white paper says that the current review of nuclear research and development within the UK Atomic Energy Authority will take into account the extent to which the customer-contractor principle can be extended in this field and goes on to say that in future the research and development by the industrial research establishments of the Department of Trade and Industry and the non-nuclear work of the UKAEA, at present worth £26 million a year, will in future be commissioned by a series of requirements boards representing government departments and industry and dealing with fields such as standards and metrology, ship technology, mechanical engineering and chemical processing. The white paper goes on to propose a strange piece of bureaucracy—a plan to set up under the Chief Scientist at the Department of Trade and Industry two separate divisions—a research and development requirements division to serve the interests of customers, and a research and development contractors division to represent the contractors.

The white paper does little to acknowledge the serious misgivings about the way in which other government departments are at present equipped to commission research and development, although it does say that the Department of Health and Social Security will appoint a chief scientist, and a small team of part-time scientists to help him. The Ministry of Agriculture is also to appoint a chief scientist, with two deputies and a small team. It is planned to set up joint consultative machinery with the Agricultural Research Council. The white paper says that the government is to review the organization of other departments, such as the Home Office and even the Foreign and Commonwealth Office, "to ensure that they are able to fulfil their functions in accordance with the customer-contractor principle and in keeping with the relatively modest scale of their research and

development programmes".

The white paper has some sensible things to say about those who work as scientists within the government machine. Acknowledging that many scientists at present become involved in management and administration as their careers develop, the government says that it will seek to encourage this trend and, with this objective, will strengthen its new programme of training and career development.

The white paper says that the belief that scientists themselves do not wish to leave the laboratory bench has been belied by recent surveys among scientific civil servants in their thirties. It suggests that past if limited experience has shown that scientists are able successfully to transfer to management and administration. The white paper does however acknowledge that uncertainty about the welcome they would get from the administrative civil service has in the past discouraged scientists from making the change, with the result that it is now planned that the Civil Service College should take the initiative in seeking out those scientists in public service who wish to become managers or policy-makers. The government says that there is likely to be a particular need for able administrators with a scientific background at the under-secretary level.

The white paper also outlines an intention to encourage more mobility between the scientific civil service proper and the research councils, universities and industry. To foster collaboration with outside interests, the Civil Service Department is therefore setting up "a high level task force" to investigate the problems involved in making transitions in and out of the civil service and eventually to develop and to administer such a scheme.

By all accounts, the government is confident that its proposals will commend themselves to the research councils. A decision on the future of the CSP will be made in the autumn, and it is intended that the government departments principally concerned will be fully equipped to commission sensible applied research long before the Chancellor of the Exchequer makes his budget speech next April. It will be widely welcomed that the chairman of the supervisory committee for the fuller use of scientists in management within the Civil Service should be Professor Herman Bondi, the most civilizing influence within the Ministry of Defence since the introduction of married quarters for other ranks. For the rest, it may well turn out to be the case that the principal value of Lord Rothschild's proposals for the reorganization of civil science is that he has served as a catalyst to bring two previously suspicious if not hostile partners into partnership.

NEW WORLD

Kennedy Bill Gains

by our Washington Correspondent

THE outlook for Senator Edward M. Kennedy's proposed National Science Policy and Priorities Act has brightened considerably. Kennedy's bill, which is one of the most far-reaching pieces of legislation on scientific matters to come before Congress for many years, has been passed unanimously by the Senate Committee on Labor and Public Welfare. And, on the other side of Capitol Hill, the bill was introduced into the House of Representatives a few days before Congress broke up for the Democratic convention by Mr John Davis, chairman of the subcommittee on Science, Research and Development.

Kennedy's bill would put the National Science Foundation squarely into the business of funding applied research, and would fundamentally change the federal pattern of research support. The bill would give the foundation some \$1,800 million to spend over the next three years on research into urban problems—health care delivery, waste disposal and mass transportation—as well as for retraining scientists and engineers thrown out of work by cutbacks on expenditure on defence and space. (See *Nature*, 237, 306; 1972 for a fuller discussion of the bill.) It is now expected to be brought before the Senate in August, but its passage through the rest of the Congressional mill hinges on what happens in the House of Representatives and on how long Congress stays in session before the November elections.

Backers of the bill are elated by the fact that all seven Republicans on the Senate Committee on Labor and Public Welfare supported it last week in spite of some vigorous lobbying by the Administration. Another indication of the bill's prospects in the Senate is the fact that it is attracting co-sponsors like a magnet—an aide to Senator Kennedy estimated last week that it will have picked up about 40 backers by the time it reaches the Senate floor. And the election could also give the bill a favourable wind.

The prospects in the House of Representatives are, however, much less clear. For one thing, a companion to Kennedy's original version of the bill—a more modest proposal which did not contain the provisions for research into urban problems—was introduced into the House more than a year ago and has since been languishing in Mr Davis's subcommittee.

After extensive hearings a year ago, the subcommittee lost interest in the bill and it dropped out of sight. Until Davis's action last week, it therefore seemed likely that the subcommittee would be content to sit on the bill, at least during election year; but much will now depend on whether the subcommittee will reopen hearings on the new version or simply approve it and send it to the full Committee on Science and Astronautics.

It is something of a surprise that a bill that would have such a considerable impact on science policy has so far excited so little interest. The Administration is opposed to it on the grounds that it would involve the National Science Foundation in projects which belong to the mission agencies. The National Science Foundation is also quietly worried about the prospects of a shift of its centre of gravity away from basic science—its traditional constituency—and about the suitability of its grants procedure for supporting applied research projects. Yet the Administration may be embarrassed, especially in an election year, in opposing a bill that would focus science and technology on domestic problems.

NIH

Support from the Senate

by our Washington Correspondent

SHORTLY before starting its short recess for the Democratic Convention, the Senate provided yet more evidence of the power of the biomedical research bandwagon in the United States. It voted to give the research institutes of the National Institutes of Health some \$1,900 million to spend in the 1973 fiscal year (which started on July 1)—\$319.5 million more than the Administration requested and \$176.7 million more than the House of Representatives allocated. Although the final amount that Congress will vote for the NIH must now be decided by a conference committee, there is no doubt that the National Institutes of Health will get much more money than they asked for. In comparison, the National Science Foundation, which has had its budget slashed by just over \$20 million (see *Nature*, 237, 423; 1972), seems particularly hard done by.

Almost every institute in the NIH complex is destined for a large budget increase if the Senate gets its way, but the chief beneficiary is the National

Heart and Lung Institute. The Senate has agreed to add \$94.7 million to the Administration's request for the NHLI, which would give the institute \$350 million to spend during the coming year. The figure, which is \$50 million more than the House of Representatives has voted, is based chiefly on the fact that diseases of the heart and lungs are the number one killers in the United States.

As for the National Cancer Institute, the Senate has agreed with the House of Representatives on a figure of \$492.2 million—\$60 million more than the Administration asked for. Even the Administration's budget would have given the National Cancer Institute some \$50 million more than it received for the 1972 fiscal year. And the Senate has also followed the lead of the House in appropriating huge increases for health manpower, particularly for the construction of new medical schools.

ASTRONOMY

Tight Job Market

by our Washington Correspondent

ASTRONOMERS are now feeling the discomforts of a tight job market and are joining other groups of scientists in the unemployment queues. The origin of their troubles is familiar—universities have expanded their astronomy departments in recent years, but as the production was cranked up to produce its maximum output, federal funding for astronomy slacked off. While two thirds of those coming out of the universities in 1967 with a PhD in astronomy could count on choosing between two or three job offers, those graduating now are happy to get a single offer. Moreover, during the past few years there has been a marked shift in the pattern of employment among new PhDs. In 1967, educational institutions soaked up 80 per cent of the crop of PhDs, but by 1970 the proportion had dropped to 37 per cent—a sign that teaching posts have now become saturated.

To see what could be done about the situation, the American Astronomical Society established a manpower and employment committee in August 1971. The committee's report (*Guidelines for Employment Opportunities in Astronomy*, available from Mr H. M. Gurin, 211 FitzRandolph Road, Princeton, NJ 08540), suggests that this year the number of new PhDs matches almost exactly the number of available jobs.

NEWS AND VIEWS

High Energy Gamma Rays from the Galactic Centre

AMONG the new astronomies which rely principally, though not entirely, on the use of space vehicles for detecting quanta that would otherwise be absorbed in the Earth's atmosphere, X-ray astronomy in particular shows promise of rivalling radio astronomy in its capacity to clarify a wide range of astrophysical problems. The importance of both the radio and X-ray spectral ranges to astronomy was established by accident during unrelated investigations. These disciplines have provided significant surprises both in the number of sources detected and in the intensity of fluxes observed. By contrast, gamma ray astronomy—say the study of quanta at energies greater than 30 MeV—began with detailed calculations of the fluxes to be expected and the first such estimates were contained in a review by P. Morrison in 1958. Observations have since shown that the fluxes are less than was predicted in some of the more optimistic calculations. Furthermore, the field has developed slowly because gamma ray sources are very faint relative to the background counting rates in the detectors that are useful at high photon energies.

Although a considerable effort has been made during the past ten years to detect high energy photons of celestial origin, there are very few positive results to hand. The first good evidence for the detection of a celestial gamma ray flux has come from the counter telescope flown on the OSO-3 satellite by Clark, Garmire and Kraushaar (*Astrophys. J.*, **150**, L203 ; 1968). This instrument detected photons at energies above 100 MeV from the neighbourhood of the galactic centre. After a recalibration of the instrument, the latest flux value of $1.2 \pm 0.3 \times 10^{-4}$ photons $\text{cm}^{-2} \text{s}^{-1} \text{rad}^{-1}$ is in acceptable agreement with the results obtained by balloon borne spark chamber experiments. One observation of the galactic centre (Frye *et al.*, *Nature*, **223**, 1320 ; 1969), however, failed to detect any excess flux over background at energies above 50 MeV. Because the width of the region emitting the gamma rays may be smaller than the detector resolution, the intensities are usually quoted in terms of a line intensity. Uncertainty about the source size coupled with the fact that the net flux value is obtained from the difference between two large numbers leads to difficulty in both the detection of fluxes and the determination of their values. Three different groups of workers have nevertheless presented evidence for high energy photon emission from the centre of our Galaxy.

There are several possible mechanisms for producing high energy photons in the galactic centre region ; cosmic ray electrons could either collide with interstellar matter to produce photons by the bremsstrahlung process or spiral in magnetic fields to radiate photons by the synchrotron process. High energy electrons could also lead to high energy photon production by interacting with the 3°K black body radiation through the inverse Compton process. Cosmic ray protons can produce neutral π mesons by collision with the interstellar gas. The π^0 mesons decay to produce pairs of gamma ray photons with a characteristic energy spectrum that permits this process to be distinguished from the other mechanisms. Fichtel *et al.*, in

addition to detecting radiation above 100 MeV from the galactic centre, established an upper limit for the radiation in the 50–100 MeV range (*Astrophys. J.*, **171**, 31 ; 1972). According to these workers, a comparison of the flux above 100 MeV with this upper limit suggests that π^0 meson decay is the source of the radiation.

One model of the galactic centre region would then be based on the suggestion that there is a source of perhaps ten degrees extent surrounding the centre in which π^0 mesons are produced by fluxes of cosmic ray protons that are large compared with the particle fluxes in other parts of the galaxy. There is, however, another possible explanation, namely that the emission arises from a number of discrete sources, of strength around 10^{-5} photons $\text{cm}^{-2} \text{s}^{-1}$ above 100 MeV that are not resolved by the OSO-3 detector or by the balloon borne spark chambers flown by Fichtel and his colleagues. The University of Southampton group—Browning, Ramsden and Wright—in their article on page 138 of this issue of *Nature* provide experimental evidence in support of this suggestion. The data were obtained with a spark chamber system that was flown from Palestine in Texas on September 21, 1971, carried on a balloon.

Three regions of anomalously high gamma ray intensity were observed near the centre of the galaxy. These sources have fluxes of around 2×10^{-5} photons $\text{cm}^{-2} \text{s}^{-1}$ and produce an excess over the background that is more than 3σ in each case. Although Clark *et al.* and Fichtel *et al.* identify only a line source of gamma rays in this region of the galactic plane, the Southampton workers point out that if the three sources which they observe were unresolved, they would give rise to a line source identical to that observed by the other two groups. After subtracting source contributions they are able to set an upper limit of 8×10^{-5} photons $\text{cm}^{-2} \text{s}^{-1} \text{rad}^{-1}$ on the line source strength along the galactic equator.

The Southampton group have recently (Browning *et al.*, *Nature Physical Science*, **235**, 129 ; 1972) detected several sources in the Cygnus region of the galactic plane, so that it may no longer be necessary to argue that the only site of observable gamma ray production is an extended region in the galactic centre. On the other hand, their possible identifications of soft X-ray counterparts for these Cygnus region gamma ray sources include the supernova remnants SN1572 and Cas A, both recent non-thermal X-ray emitting objects, and the Cygnus Loop which is a much older remnant ($\sim 5 \times 10^4$ years) emitting its X-rays thermally from the shock heated interstellar plasma. The three galactic centre gamma ray source positions include three soft X-ray sources. One of these (2U1813–14) coincides with a weak variable radio source and is therefore likely to be a binary system with a degenerate member. It is difficult to see the emission of high energy gamma rays as a common feature of all these objects. As the angular resolution and sensitivity of gamma ray telescopes improve, however, more information will be obtained which should strengthen and clarify the relationships between the new astronomies.—From a Correspondent.

Ceramics based on Silicon Nitride

SILICON nitride (Si_3N_4) is a highly promising material for application in high-temperature engineering and other fields, because of its unusual combination of properties and because of the variety of fabrication methods now available which, used singly or together, allow its production in complex shapes. Indeed this ceramic is currently the subject of intense interest and activity with much of the stimulus coming from the possibility that improved automobile engines might be made almost exclusively from it.

A new dimension has now been opened up in that it has been established that the crystal lattice of this nitride can accommodate other atoms, both metallic and non-metallic, in large amount. Parallel work in Japan and the United Kingdom has shown that aluminium and oxygen can enter the $\beta\text{-Si}_3\text{N}_4$ lattice (to give a solid solution of alumina (Al_2O_3) in the nitride), and it is also clear that metal atoms of low valency, such as lithium and magnesium, can enter as well, in a charge-compensating role. A preliminary statement on important work in this new area is given by K. H. Jack and W. I. Wilson (*Nature Physical Science*, **238**, 28; 1972), who report not only details of the crystal chemistry but also information on fabrication and properties. Particularly noteworthy are the findings that the nitride can accommodate more than 65 per cent by weight of alumina, that the thermal expansion of the solid solution can actually be smaller than that of the pure nitride (already small, giving good resistance to thermal shock), and that solid material can be fabricated by sintering powder (the traditional fabrication route for ceramics, but which cannot be used with silicon nitride itself).

Silicon nitride, and the new solid solutions based upon it, are truly synthetic ceramics. Apart from the fabrication of the solid from the particulate state, the starting powder itself has to be synthesized: neither the nitride nor the Si-N-Al-O solid solutions are natural minerals, although all the constituent atoms occur frequently in the Earth's crust or atmosphere. Although it was known in the eighteenth century that silicon and nitrogen could be made to combine, it was not until the 1950s that silicon nitride ceramic was developed. Engineering exploitation of this ceramic was pioneered in the late 1950s and 1960s, largely in the United Kingdom, with the effort led by N. L. Parr and his colleagues at the Admiralty Materials Laboratory, Holton Heath, and with important parallel work on the ceramic science of the material by P. Popper and his colleagues at the British Ceramic Research Association.

Even at this early stage there was interest in the possibility of using silicon nitride in the stator, and maybe also the rotor, blades of aircraft gas turbines (no new goal for ceramics, application of alumina, metal-bonded carbides and other materials having previously been attempted unsuccessfully following initial German work in the Second World War). Development of the nitride has been pursued with many other applications in mind, including flame cans and other parts of turbines, high-temperature gas bearings, welding jigs and containers for molten metal. Silicon nitride has been more attractive than other ceramics because of its exceptional re-

sistance to failure by thermal shock, its reasonable strength at all temperatures up to about $1,200^\circ\text{C}$, its specific gravity (approximately 3), its high hardness and generally low coefficient of friction, and its good chemical stability, including resistance to oxidation at temperatures up to at least $1,200^\circ\text{C}$.

The variety of silicon nitride used in the early work on engineering exploitation was "reaction sintered", meaning in this case that the shape required was first formed in silicon, rather than silicon nitride, powder, the pre-form then being converted to the nitride and consolidated by heating in nitrogen. This fabrication route has an unusual and highly advantageous feature: there is essentially no volume change during nitridation of the silicon pre-form and, as conventional tooling is suitable for machining partially-nitrided material, the fully-nitrided ceramic can easily be made to close dimensional tolerances. Nowadays there are many ways of preparing the silicon pre-form (that is, before any machining that may be desired), including by die pressing, isostatic pressing, slip casting, flame spraying, and incorporation of polymeric material followed by some suitable procedure such as injection moulding. This wide range of forming methods now allows production of far more complicated shapes in silicon nitride than is usually possible with ceramic materials.

Reaction-sintered silicon nitride is always porous on a micro-scale (voidage about 20 per cent). Pore-free material can also be made, by hot pressing, and the elimination of the porosity gives increase in strength (from 200 to $>700\text{ MNm}^{-2}$, 30,000 to $>100,000\text{ p.s.i.}$ in bend), increased resistance to chemical attack, and improvement in other properties. The fabrication of silicon nitride by hot pressing was first reported in 1961 by G. G. Deeley, J. M. Herbert and N. C. Moore of the Plessey Research Centre, Caswell. This high quality, but expensive, variety of the nitride also has high potentiality for engineering application.

Following only modest effort during more than a decade, the scale of research and development activity directed towards engineering application of silicon nitride has both increased dramatically and spread overseas during the past four years. This was clearly evident from a meeting of the Basic Science Section of the British Ceramic Society held at Cambridge on July 4-6 and organized by D. J. Godfrey of the Admiralty Materials Laboratory, at which no less than twenty-one papers, wholly or partly devoted to silicon nitride, were presented, and at which more than a quarter of the participants came from abroad. The accounts given of the large effort on exploitation of silicon nitride now being mounted in the United States, at the Ford Motor, Westinghouse and Norton companies, were particularly impressive. One speaker, probably in a better position to know than any other participant, declared that it is now a "virtual certainty" that ceramics can be applied both in small (automobile) and large land-based turbines. The meeting also served to emphasize the urgent need to improve understanding of the basic science of silicon nitride and related materials.

The work of K. H. Jack and his colleagues at the University of Newcastle upon Tyne on the new solid

solutions based on β - Si_3N_4 was reported to the meeting, and it was generally agreed that it showed the way forward to development of a range of new and promising materials. The ability of at least some of the solid solutions to densify during sintering without application of pressure or resort to reaction sintering will be an important advantage, although this must be at the expense of the unusual advantage of the close dimensional control associated with the reaction-sintering route. Preliminary information suggests that the thermal shock resistance of the new materials can indeed be good, and that they will not be deficient in strength. Corrosion resistance is highly promising, both with oxygen and with several molten metals at high temperature.

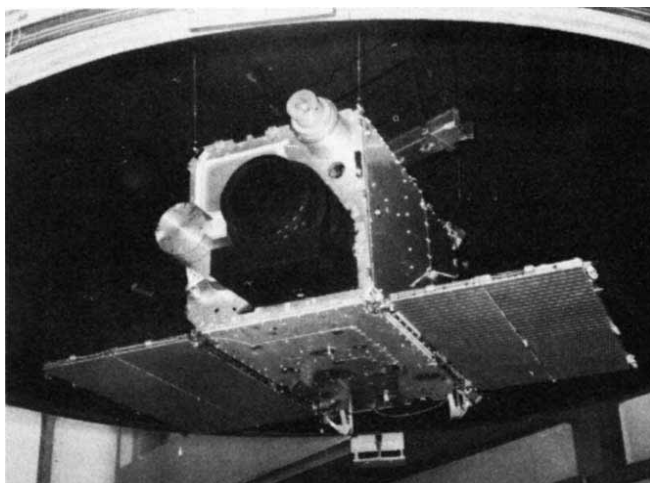
The most intriguing aspect of these new results, however, is the extensive range of compositions in the Si-Al-N-O and related systems that can clearly exist as single phases. There is close analogy with the family of silicates, both crystalline and vitreous. The structure of β -silicon nitride is based on SiN_4 tetrahedra joined at their corners (in threes). The substitution of aluminium for silicon now proved in this nitride is commonplace in the SiO_4 tetrahedra of the silicates, and incorporation of charge-compensating metal atoms of low valency is also familiar with the silicates. Substitution of oxygen for nitrogen in the SiN_4 tetrahedra of the nitride gives additional flexibility of composition. Thus, in essence, the new dimension in silicon nitride science and technology is the emergence of new materials built up of $(\text{SiAl})(\text{N,O})_4$ tetrahedra joined by sharing corners, just as silicates are built up of SiO_4 and $(\text{Si,Al})\text{O}_4$ units.—From a Correspondent.

First Data from TD-1A

THE ultraviolet sky-scan telescope on board the European satellite TD-1A has been operational for almost four months (see *Nature*, **236**, 90; 1972) and the first data now reported by R. Wilson *et al.* in this week's *Nature Physical Science* (**238**, 34; 1972) indicate that the telescope is working satisfactorily. The spacecraft was developed and prepared by the European Space Research Organization (ESRO) and its contractors in Britain and Belgium; the ultraviolet sky-scan telescope, the largest of the seven experiments on board, is the joint responsibility of teams from Britain and Belgium.

The first ultraviolet stellar spectra were obtained in 1965 from a stabilized Aerobee rocket. Accurate pointing of optical axes, or at least something to compensate for motion, is required in both rocket and satellite experiments in order to achieve passbands of about 35 Å. For TD-1A the motion of the spacecraft causes the spectrum to sweep across three exit slits to provide sixty dated points in 3.3 s from 1350 Å to 2550 Å of every star detected.

The orbit of TD-1A is synchronous with the Sun, and the optical axis of the experiment always points away from the Earth. A thorough survey of the sky is therefore completed every six months. The preliminary results show data of good quality with every indication of them being reproducible—the spectral flux measurements reported are consistent to ± 3 per cent. An ex-



Structural model of ESRO's TD-1A satellite suspended in position before space simulation tests at the European Space Research and Technology Centre, Noordwijk, Netherlands.

tinction curve for γ Columbae is presented which agrees well with some of the data obtained from the OAO-2A satellite.

Ultraviolet astronomy is important because many of the resonance lines of the elements—prime indicators of the physics and chemistry of the media under observation—lie in the ultraviolet wavelength region. Data on the hotter stars, which have much shorter lives than stars such as the Sun, also become available from such observations. The interstellar medium may also be investigated by using the bright ultraviolet stars as background sources and observing absorption effects. For these reasons, ultraviolet astronomy has differed from X-ray astronomy in that emissions detected in the ultraviolet were predictable before the first measurements. There is the possibility, however, that some of the more exotic sources—for example the pulsating sources Centaurus X-3 and Hercules X-1, and Cygnus X-1 and Scorpius X-1—discovered by X-ray astronomers may also emit ultraviolet radiation. Ultraviolet spectra of these objects may help to throw more light on the operational mechanisms.

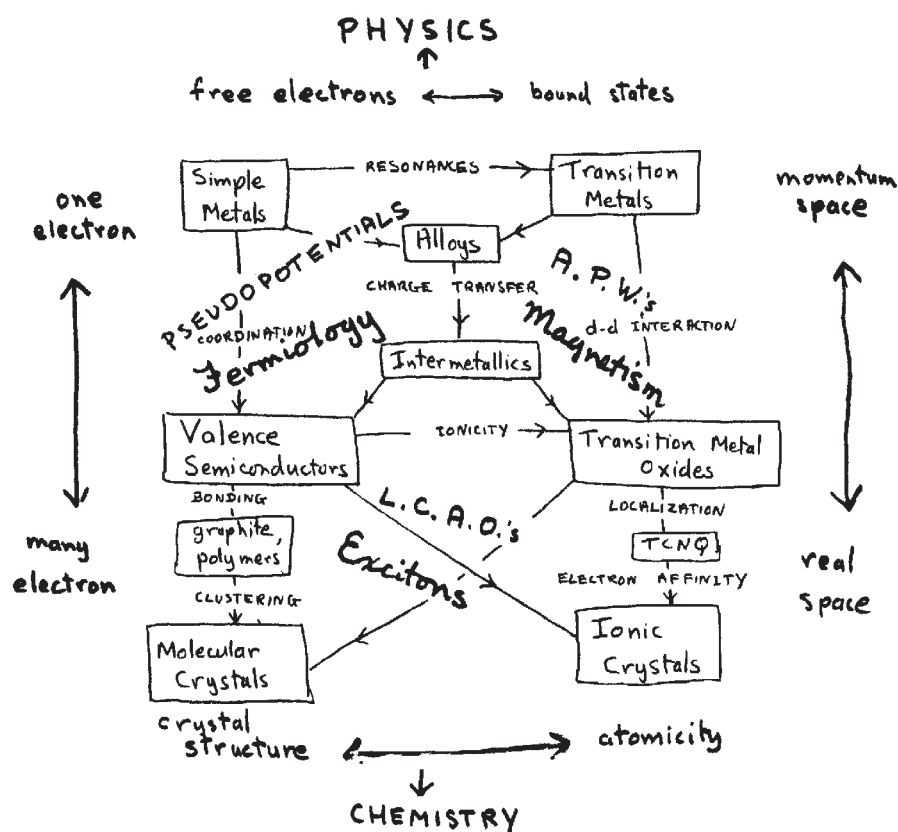
A previous satellite experiment on OAO-2A for observing ultraviolet radiation has proved interesting in that several objects radiate more in the ultraviolet regions than was expected. These Orbiting Astronomical Observations concentrate in particular on ultraviolet radiation and provide a stable platform from which detailed observations may be made. Unfortunately, the launch of OAO-B was a failure, but OAO-C, with an ultraviolet experimental package from Princeton University on board, is due to be launched next month. A joint University of London/University of Leicester X-ray telescope will also be on board and pointing in the same direction and will complement the Princeton experiment.

The ultraviolet sky-scan telescope on TD-1A will provide a useful survey of the sky and it is hoped that 20,000 stars, of which 6,000 will give usable spectra, will be detected. The OAO satellite experiments cannot hope to match this, but the detailed spectra may be better. Exciting data from the ultraviolet sky may thus become available from these complementary satellites during the next few months.—From a Correspondent.

SOLID STATE PHYSICS

An Annotated Doodle

from a Correspondent



Caption.

International Conference on Band Structure of Solids, July 3-6, 1972. University of Exeter: Institute of Physics and International Union of Pure and Applied Physics.

Notes.

An unusually wide range of materials was considered and a new conceptual synthesis achieved:

- Many new spectroscopic techniques, of greatly improved sensitivity, are now being used including ultraviolet spectroscopy, X-ray emission and absorption, ultraviolet and X-ray photoemission, spin-polarized electron emission, isochromat X-ray emission, inelastic electron scattering, and polarized positron annihilation. Band structures are now being probed in depth with precisions of a fraction of a volt. Modulation techniques discover interesting new features in the higher derivatives of the spectrum. Experiment is well ahead of theory.

- Bands can arise from atomic characteristics (d-levels, electron affinity) or from the geometrical arrangement of atoms in space (crystal lattice, coordination, bonding, clustering).

- Any good band structure "method" can be used to compute the Bloch states in any one-electron periodic potential. But the optimum method as between

pseudopotentials, "APWs" (that is, including KKR) and LCAOs follows the gradient from free electrons, through d-resonance, to atomic or molecular bound states.

- The characteristic one-electron phenomena of simple metals ("Fermiology", as in the de Haas-van Alphen effect) give place to strong, local, exchange and correlation interactions (magnetism) and eventually to collective electron spectra of ions and molecules (excitons). How much do these phenomena overlap and co-exist?

- Simple screening and charge transfer models are inadequate to explain bonding, localization and ionicity. Are sophisticated local density methods, such as "X-alchemy", going to be adequate for this many-body problem? What questions are answered by computations with adjustable parameters? Are *ab initio* calculations worth their cost?

- The gradient from momentum space representations ("Fermiology") to real space representations (clustering, localization) crosses the frontier between physics and chemistry. Intermediate systems (graphite, polymers, TCNQ) are especially interesting.

- Disorder is a third dimension of experiment and theory. Liquid metals retain their one-electron properties, but

the destruction of long range order in amorphous semiconductors has less drastic effects on the electronic spectrum than might be supposed.

DNA REPLICATION

Unfolding Agents

from our Molecular Biology Correspondent

DOUBLE helical DNA is an extremely stable structure, and must yet be able to open up under physiological conditions when it is called on to do something biologically interesting, such as replicating. One of nature's ways of facilitating this kind of operation is to provide an agent that binds to the single stranded conformation, and so diminishes the stability difference between this and the base-paired state. The most striking and best documented example of a molecule endowed with this property is the gene 32 protein of T4 bacteriophage, unearthed by Alberts. This binds strongly to single stranded DNAs, and is indispensable both for DNA replication in infected cells and for genetic recombination, which involves fusion of two double helical DNA molecules. Some striking pictures of the gene 32 protein at work have now been obtained by electron microscopy by Delius, Mantell and Alberts (*J. Mol. Biol.*, **67**, 341; 1972).

The binding of the protein to single stranded DNA is highly cooperative, and the combining ratios are such that one would expect the DNA to be completely coated. The sedimentation properties of the complex also suggest a rather stiff structure, and this is borne out by electron micrographs of the particles, fixed with glutaraldehyde and spread on cytochrome monolayers. The DNA strands appear thicker than double helices, and the contour lengths correspond to an extension of 4.6 Å per nucleotide. The cooperativity of binding shows up in the form of alternating stretches of covered and bare DNA, when the concentration of protein is below the equivalence value.

Now it seems that the gene 32 protein binds by preference to regions rich in A and T, for in the alternating polymer, poly (dA-T), it brings the melting point of the double helix down to about room temperature. Delius *et al.* have tested this proposition by adding the protein to λ-phage DNA, exposing the complex to a temperature at which the DNA is partially melted, fixing the melted regions and examining a population of molecules so treated in the electron microscope. This in fact is Inman's procedure for compilation of melting maps, which reflect the distribution of A-T rich regions of DNA. In λ-phage DNA there is a particularly marked polarization of composition, so that in

the early stages of melting, almost everything happens in one half of the molecule. In the presence of the unwinding agent, the melted segments appear much thicker than in the partially uncomplexed DNA which shows that they are encrusted with protein.

When the denaturation map for melting at 37° in the presence of the protein is plotted out, it is seen to be essentially identical to that of λ -DNA alone, after exposure to heat or alkali, with several well defined denaturation-prone regions in the A-T rich half of the molecule. In supercoiled circular SV40 DNA, the gene 32 protein caused the formation of loops of denatured material. By the introduction of ethidium bromide, which intercalates between the bases, thus stretching the double helix and generating slack, it is possible to sort intact supercoils from those containing single strand nicks. By this criterion it is found that the gene 32 protein generates loops most readily in intact supercoiled chains. Thus the slack, or underwinding, which characterizes this supercoiled DNA favours binding of the protein, with consequent release of the corresponding structural strain in the double helix.

Just how the gene 32 protein directs the DNA replication process is not known, though it is established that other proteins are present in the replication complex, which may modify its unfolding propensity and specificity. As to genetic recombination, one must suppose that by bringing both participant molecules close to their melting conditions, the protein permits an annealing process to occur (single strand breaks having first presumably been introduced). The denaturation mapping technique offers, as Delius *et al.* point out, a ready-made criterion for the identification of unwinding proteins from various systems, among which are already numbered the filamentous bacteriophages and calf thymus. Other DNA-binding proteins that are trapped on DNA-containing columns evidently do not generate the characteristic co-operative complexes, and are therefore not functionally related.

A protein of a different kind, though with an effect on DNA conformation, was recognized in the *Bacillus subtilis* phage, ϕ 29, by Vinuela, Salas and their colleagues. The protein is evidently responsible for non-covalent cyclization of the linear phage DNA, which reverts to its linear state after treatment with trypsin. Hirokawa (*Proc. US Nat. Acad. Sci.*, **69**, 1555; 1972) has now found that its protein complement is indispensable for infectivity of ϕ 29 DNA. After proteolysis, which is accompanied by a distinct change in buoyant density, the activity vanishes. By introducing trypsin at various stages of transfection experiments, Hirokawa has obtained

evidence that the protein is required for the initial association of the DNA with the receptor sites of the cell, and that it is therefore, as might be expected from its ability to cyclize the DNA, attached at the end of the chain. Hirokawa infers from reactivity towards nucleases that this end may well be single stranded though the failure of the protein-free molecule to cyclize seems to exclude paired single stranded ends as in λ -DNA.

MARINE BIOLOGY

Sector Scanner Scores

from a Correspondent

A JOINT meeting of the Challenger Society and representatives of marine laboratories was held in the University of East Anglia on July 4 to 6. Nineteen contributions by members of staff of the Lowestoft and Burnham Fishery Laboratories of the British Ministry of Agriculture, Fisheries and Food served to illustrate the diversity of research activities in these laboratories; indeed they covered the whole spectrum of marine science from biochemistry and genetics, through physiology, population dynamics, radiochemistry and physical oceanography, to commercial fisheries and gravel dredging.

The classical problem of recognition of fish stocks was tackled from opposing biochemical and morphological angles by Dr A. Jamieson and Dr C. E.

Purdum; this subject came up again in a contribution, on the horse mackerel, by Mr C. T. Macer who uses plots of otolith weight against fish length to distinguish between stocks. Dr R. C. A. Bannister argued that the present catches of plaice in the North Sea are close to the maximum sustainable yield; the increases in catches during the past ten or fifteen years have given practical proof of the efficacy of conservation measures and of the theories advanced earlier by Beverton and Holt.

Mr M. G. Pawson described his search for the active constituent of the lugworm which attracts their prey, the whiting. Glycine is the most effective attractant, followed by alanine. In some of his experiments Mr Pawson has been able to compile a "synthetic" lugworm consisting of amino-acids mixed in the same proportions as those in which they are found in the lugworm. Dr P. R. Winslade described experiments on the swimming and resting behaviour of the sandeel, *Ammodytes marinus*, under various conditions of light, temperature and food. He has discovered that sandeels burrow into the sand in the dark and argued that this is why the commercial fishery is successful only during the day when the sandeels emerge and swim above the bottom (whereas some fishery biologists had previously suggested that they swam near the surface at night—above the nets).

Two quite different contributions demonstrated the extraordinary pre-

Cooperativity in Actin Filaments

COOPERATIVITY in biochemical systems is a phenomenon which is currently being extensively investigated. A particularly clear example which may point the way towards the kind of solution to be expected to the problem has been found in muscle and is described by Bremel and Weber in next Wednesday's *Nature New Biology* (July 26).

Muscle contracts when the myosin heads projecting from the thick filaments attach to the actin subunits of the thin filaments and, by an unknown mechanism, impress a longitudinal force on them which causes the two types of filaments to slide past each other. The contraction process requires the presence of ATP and calcium. In the absence of ATP the muscle goes into rigor when the two sets of filaments are firmly bound together by all the myosin heads attached to the thin filaments. If a high concentration (15 mM) of ATP is added in the absence of calcium the myosin heads detach and the muscle relaxes. If calcium and ATP are present the muscle begins to hydrolyse ATP and contraction occurs.

Ebashi found that in vertebrate

striated muscle there is a regulating system on the thin filaments. This consists of two proteins—tropomyosin and troponin—which together with actin make up the thin filaments of vertebrate striated muscle. The ATPase activity of myosin is enhanced by actin but is inhibited by the tropomyosin-troponin system. When calcium is bound to troponin the inhibiting power of the tropomyosin-troponin disappears and the ATPase activity of myosin increases.

Bremel and Weber have studied the binding of calcium to troponin in myofibrils at two different ATP concentrations and in synthetic regulated thin filaments in the presence and absence of myosin. They have also examined the ATP dependence of the actin-activated ATP hydrolysis of the enzymatic subfragment of myosin in the presence and absence of calcium and find that when actin molecules are bound to myosin, as in rigor in the absence of ATP, troponin binds calcium more strongly and the remaining unbound actin molecules are made available for interaction with myosin even though calcium is absent.

cision of the sector scanner developed by the Admiralty Research Laboratory at Teddington, Middlesex. Dr F. R. Harden Jones has liberated tagged plaice at sea and tracked them with the sector scanner as they were trawled. He, and his colleagues from the Lowestoft Laboratory, have tracked and trawled seventy-five fish so far; their results, dramatically recorded on film, are revealing a great deal that was unknown, or speculative, about the behaviour of fish in the vicinity of otter boards, tickler chains, bridles, foot ropes and all the paraphernalia of commercial trawling. Their preliminary results suggest that nearly half of the fish between the boards and more than 60 per cent of those in the path of the net are caught without the use of door-to-door ticklers. Dr R. R. Dickson gave an account of the ARL sector scanner which he has used in studies of gravel dredging. It is possible to pick up a dredged trench only six inches deep and two or three feet wide at a range of 120 yards. Exploratory holes and exploited patches of gravel are easily detected; the sector-scanning image is so clear that different holes can be clearly identified and found again on subsequent cruises. The results suggest that the holes and trenches made by gravel dredging may not be filled in by natural turbulence and movement of the neighbouring seabed. There can be little doubt that the sector scanner is a research tool of the greatest importance.

The special lecture was given by Professor J. A. Kitching (University of East Anglia) who described the programme of ecological studies by staff and students from the Universities of Cork, Bristol, East Anglia and elsewhere who have worked in and around Loch Ine for more than thirty years. Dr G. C. Kearn (University of East Anglia) described his field and experimental search for the means by which the free-living larvae of *Entobdella solei*, a parasite of the common sole, find their way to their hosts. The sole is active at night but buries itself in the sand and remains stationary for most of the day. The eggs of the parasite, which fall to the bottom, hatch soon after daylight, and Dr Kearn has been able to show that they are attracted, presumably by a chemo-perceptive mechanism, to the skin of the sole. Another speaker from the University of East Anglia, Dr I. N. McCave, attempted a budget for the deposition of mud in the North Sea. His results emphasized the need for much more information about the volumes and rates of transport of sediments out of estuaries. It was apparent from the discussion that more needs to be discovered about the effects of dumping and sewage effluent; these may not be inconsiderable sources of sediments on the floor of the seas.

MOLUCULAR GENETICS

UAA in Eukaryotes

from our Cell Biology Correspondent

THE belief that the genetic code is universal to all prokaryotes and eukaryotes, even though almost all the direct evidence for particular codon assignments has come from experiments with *Escherichia coli* and its phages, is, of course, a cardinal tenet of molecular biologists. And the faithful will no doubt be reassured of the inviolability of their doctrines by what Stewart, Sherman, Jackson, Thomas and Shipman have to say in the current issue of the *Journal of Molecular Biology* (67, 83; 1972). This group, pursuing their penetrating and exemplary analysis of the molecular genetics of the cytochrome *c* in baker's yeast, have now established that in this eukaryote, as in *E. coli*, the codon UAA acts as a nonsense codon terminating the synthesis of polypeptides.

Stewart *et al.*'s unequivocal evidence comes from a detailed investigation of the properties of strains carrying a particular mutant designated *cyl-9*, and of a large set of revertant strains. Yeasts carrying the *cyl-9* mutation contain the normal amount of iso-2-cytochrome *c*, but they contain less than 0.5 per cent of the normal amount of iso-1-cytochrome *c*. Clearly this mutation must

either prevent the synthesis of this cytochrome or it must cause the very rapid degradation of this protein. This property of strains carrying the *cyl-9* mutation, together with the fact that the *cyl-9* mutation is suppressible (Gilmore, Stewart and Sherman, 1971), is, of course, redolent of the properties of strains of *E. coli* carrying amber or ochre mutations in structural genes; and to establish that the *cyl-9* mutation results in the generation of an ochre codon in the structural gene for iso-1-cytochrome *c* Stewart *et al.* have exploited methods made familiar by bacterial geneticists.

In essence Stewart *et al.* have isolated spontaneous and induced revertants of *cyl-9* mutant strains and have determined the amino-acid composition and amino-terminal sequence of the cytochromes they specify. By virtue of their composition the iso-1-cytochrome *c* molecules made by the revertant strains fall into five classes; those with the normal composition and those with one glutamic acid residue replaced by either one lysine, serine, leucine or tyrosine residue. Analysis of peptide maps of cytochromes of these five classes reveals that the glutamic acid that has been substituted is the second residue in the polypeptide chain immediately following the amino-terminal threonine residue. Furthermore, the chymotryptic

Viral Messengers and Poly A

ALTHOUGH it would be erroneous to make the generalization that all eukaryotic messenger RNA molecules have at their 3' ends a run of between 100–200 adenylic acid residues—putative histone messengers do not—the tally of mRNAs known to have such a 3' poly A sequence grows almost daily. In *Nature New Biology* next Wednesday (July 26), for example, Weinberg, Ben Ishai and Newbold and Eaton, Donaghue and Faulkner report respectively the presence of poly A tracts in SV40 and Sindbis virus messengers.

Weinberg *et al.* find that SV40 messengers in cytoplasmic polysomes in permissive, monkey BSC1 cells during replication of the virus terminate in a tract of about 150–200 bases, at least 90 per cent of which are adenylic acid. This tract must be added to the messengers after transcription because the viral DNA does not contain more than twenty consecutive A=T base pairs. Likewise in non-permissive mouse 3T3 cells transformed by SV40 cytoplasmic messengers containing sequences specified by the resident transforming SV40 genome terminate in a similar poly A tract. Furthermore, in infected cells heterogeneous nuclear RNA molecules containing viral sequences and believed to be precursors of the viral messengers

found in cytoplasmic polysomes also terminate in a 3' poly A tract. It seems therefore that the cellular enzyme(s) in the nucleus responsible for adding poly A to messenger precursor molecules does not distinguish between RNAs specified by the cell and the viral genomes.

Sindbis virus, unlike SV40, has a single stranded RNA genome, and in extracts of infected cells two major and several minor species of viral RNA have been identified by gel electrophoresis. To obtain Sindbis mRNAs Eaton *et al.* isolated polysomes from infected cells, dissociated them and disrupted the ribonucleoprotein that was released to leave naked RNA which they analysed by centrifugation through sucrose gradients. These viral RNAs sediment at 4S, 16–28S and 42S. Digestion of the 16–28S RNA by pancreatic and T₁ ribonuclease liberates a resistant fragment which sediments at 3–4S and contains 75 per cent adenylic acid.

Sindbis mRNAs, which are synthesized in the cytoplasm off an RNA template, thus seem to contain poly A tracts. Whether these tracts are coded by the viral genome rather than added after transcription remains to be seen, although Eaton *et al.* suggest the former situation may well be the case.

peptides of some of the revertant cytochromes have glutamine rather than glutamic acid at the second position. The amino-terminal tripeptides therefore have the composition Thr-Glu(Gln, Lys, Ser, Leu, Tyr)-Phe.

These six amino-acids that can occur at position two of the iso-1-cytochrome *c* molecule comprise the complete set of amino-acids the codons of which, assuming the bacterial genetic code to be universal, can be generated by changing a single base of the UAA ochre codon. Moreover the codons of these six amino-acids, and one other codon which specifies in bacteria tryptophan, can be generated by changing a single base of the UAG amber codon. None of the forty-five revertant iso-1-cytochrome *c* molecules, however, has tryptophan as the second amino-acid in place of glutamic acid. It seems, therefore, that the *cyl-9* mutation results in the generation of a UAA ochre codon (rather than a UAG codon) from a GAA glutamic acid codon by the substitution in the DNA of a G.C base pair by an A.T base pair.

These results clearly indicate that the UAA codon is a nonsense chain terminator in yeast; they also suggest that the UGA codon is another chain terminator in eukaryotes as it is in bacteria. This can be explained by the fact that one of the revertants of *cyl-9* mutants should specify a UGA codon in place of the UAA, so either this codon specifies one of the six amino-acids found at the second position or more likely such revertants would be missed because phenotypically they would retain the mutant phenotype and lack iso-1-cytochrome *c*.

Stewart *et al.* round off this classic set of experiments by pointing out that the presence of the UAA codon at position two seems effectively to block reinitiation of translation at a AUG codon which can be generated at position four by mutating the wild type AAG lysine codon to an AUG triplet. By contrast, in strains which carry an AUG codon at position four, the wild type GAA codon at position two and which lack the normal AUG initiation codon, iso-1-cytochrome *c* molecules lacking the first four amino-acids of the wild type protein are made. Why and how an ochre codon at position two blocks reinitiation at an AUG codon at position four is not yet understood.

MAMMALS

Protective Porpoises

from a Correspondent

PARTICIPANTS in the fifty-second annual meeting of the American Society of Mammalogists at Tampa, Florida, on June 18–22 learnt that porpoises can be used to defend swimmers from the

devastating attacks of sharks in ocean waters. Dr P. Gilbert (Mote Marine Laboratory, Sarasota, Florida) has found that these small whales can be trained to attack and drive away threatening sharks. The training procedure which he used during 1970–71 involved the rewarding of a porpoise with food each time it took an aggressive action toward a shark also living in the training tank. Small sharks were used at first, and gradually larger animals were substituted as the porpoise learned the desired aggressive response.

Dr Gilbert's presentation was one of the highlights of the mammalogists' meeting, at which about a hundred reports were heard, dealing chiefly with North American mammals, although Australia, South America and the Middle East were also represented. During a symposium on the ecology and behaviour of tropical mammals, organized by Dr J. F. Eisenberg (National Zoological Park, Washington DC), participants dealt with such diverse examples as tree sloths (family Brady-

podidae), agoutis (*Dasyproctidae*), langurs (*Cercopithecidae*) and bats (*Phyllostomatidae*, *Molossidae* and *Desmodontidae*). Dr D. E. Wilson (National Museum, Washington DC) reported that the reproductive behaviour of most neotropical bats can be grouped into four categories: (1) aseasonal polyoestry, (2) seasonal polyoestry, (3) bimodal polyoestry and (4) seasonal monoestry. The limiting factor in the number of breeding periods each year was postulated to be food supply. Insectivorous bats tend to base their cycles on seasonal fluctuations in insect populations. Frugivorous bats take advantage of seasonal trends in fruit abundance to produce young. Blood-feeding vampire bats, however, breed continually in response to a seasonally steady food supply.

Dr N. Smythe's contribution to the symposium was a discussion of the function of territoriality in the agouti (*Dasyprocta punctata*) in Panama. He has found that these tropical rodents cooperate in defending group territories

Is β Persei a Transient X-Ray Star?

SINCE the discovery at the end of 1971 that the eclipsing binary β Persei is a radio star (*Nature*, **235**, 270; 1972), it has become apparent that there are occasional radio flares with a half-life decay of about 4 h (*Nature Physical Science*, **236**, 42 and 43; 1972). In next Monday's *Nature Physical Science* (July 24), R. M. Hjellming of the National Radio Astronomy Observatory at Green Bank, West Virginia, argues that the simplest interpretation of the data so far collected for the flaring of β Persei is in terms of a variable thermal bremsstrahlung source and, on the basis of the model which he constructs to account for the radiation during flares, Hjellming concludes that when a radio flare is at its peak, the temperature in the plasma responsible must be so high that X-rays must be produced as well. In short, β Persei should be a variable X-ray source.

On this argument, it is not, however, surprising that X-ray emission from β Persei has been missed by recent sky surveys for X-ray sources, for the flaring of β Persei and similar stars seems to be a rare phenomenon— β Persei seems to have become active at some point between the first discovery of radio emission last November and January this year, and the transition was accompanied by marked changes of radio behaviour and by the appearance of optical emission lines not previously observed.

The notion that bremsstrahlung is concerned in the radio emission from β Persei comes from the flatness of the spectrum up to 10.52 GHz, and the

tendency for the flux at higher frequencies to be proportionately greater during flares. Hjellming also points out that the optical emission lines from β Persei are not as strong as they would be if the radio emission was thermal in character and produced by a gas with a temperature of the order of 10,000 K.

With the measured properties of the radio flares as a starting point, Hjellming proceeds to calculate limits for the physical properties of the plasma that produces the radio noise. The two closely linked stars in β Persei are each about 0.03 AU in diameter and the semi-major axis to their orbit about 0.2 AU. The upper and lower limits which Hjellming calculates put the size of the emitting region during flares between 0.1 AU and 13 AU, in which case the upper and lower limits for the electron temperature are respectively 2×10^9 K and 2.5×10^5 K. His own estimate of the electron temperature at flare maxima is 10^8 K, corresponding to an electron density of 10^{10} cm^{-3} in an emitting region with dimensions of the order of 0.3 AU.

These conditions are sufficiently extreme for X-ray production to be copious, and indeed Hjellming estimates that the energy output at flare peaks may be of the order of 2×10^{35} ergs s⁻¹. He makes no estimate of the accompanying loss of mass from the system, which may be very high. His calculation will no doubt stimulate a search for X-ray emission from stars such as β Persei in the hours immediately after radio flares have been first detected, and also an investigation of transient X-ray sources such as Centaurus X-2.

which consist of areas where they have scatterhoarded seeds. He cited three advantages of this type of territory to agoutis: (1) interspecific and intra-specific competition are reduced, (2) during the reproductive season breeding animals are assured of a food supply, and (3) young animals are produced at a time when their survival is maximized.

Dr N. A. Muckenhirn (University of Maryland) reported the phenology of important food trees of the langur (*Presbytis senex*) in Ceylon. He has found that the feeding habits of these mammals shift seasonally from species to species, depending on the leaf, flower or fruit condition of the trees.

Drs G. G. Montgomery (University of Minnesota) and M. E. Sunquist reported radiotracking studies of the three-toed sloth (*Bradypus tridactylus*) during an eighteen month study conducted in Panama. Adult tree sloths confine themselves to rather limited home ranges consisting of a few adjacent trees in the tropical forest canopy. Of particular interest was the manner in which young sloths acquired their home ranges. After weaning their young, female sloths leave the offspring to occupy their home range area, while they migrate to another part of the forest.

OCEANOGRAPHY

Dispersal of Pollutants

from a Correspondent

THE general situation created by man's discharge of pollutants is well recognized, but many difficult problems have to be solved before it will be possible to give precise predictions of the effects of some of these discharges on the receiving ecosystems. Such problems occur particularly in coastal areas, and a symposium arranged by the International Council for the Exploration of the Sea was held from July 4 to 7 at the University of Aarhus, Denmark, to consider the physical processes responsible for dispersal in the sea, with particular reference to the nearshore zone.

Dispersal processes in the open sea seem to have much in common, but the dominant processes in nearshore zones may vary markedly from area to area. Thus Dr A. Okubo (Johns Hopkins University, Chesapeake Bay Institute) based his summary of information on diffusion in the sea on the notion of a spectrum of turbulence and the four-thirds power law, an idea which was also evident in work reported for the Baltic Sea by Dr A. M. Aitsam (Tallin Polytechnic Institute) and others. On the other hand, Mr J. W. Talbot (Fisheries Laboratory, Lowestoft) reported that in many English coastal areas, and even in the southern part of

the North Sea, horizontal turbulence is often of secondary importance. In these areas dispersal is controlled by vertical shear diffusion and circulation effects.

Although understanding of the processes of horizontal diffusion in the surface layer of the open sea is now adequate for most practical purposes, it was emphasized by Dr J. Joseph (International Atomic Energy Authority, Monaco) that this is not the case for diffusion near the seafloor in deep water. An account was given of the first attempt at measurement of diffusion in the deep ocean by Dr T. E. Ewart (University of Washington) who has released rhodamine B at a depth of 1,000 m and, using an acoustically controlled submersible, has succeeded in detecting the dye distribution after a period of five hours. Although this work is attended by great difficulties, it has possibilities in the future.

Another important area of study is that of vertical diffusion under various conditions, including the fine density structure that occurs in some sea areas, and some measurements of vertical diffusion in stratified conditions were reported by Dr G. Kullenberg (Institute for Physical Oceanography, Copenhagen).

In shallow nearshore areas, improved instrumentation for field measurements and developments in mathematical modelling are now enabling more detailed studies of the circulation. It is therefore becoming possible to treat as advection some processes which have previously been included as turbulent diffusion, a procedure which often led to difficulty in the determination of the diffusion parameter. Dr J. J. Leen-

MEDICAL RESEARCH COUNCIL

New Unit

A NEW Unit of Reproductive Biology is being established by the Medical Research Council in the Department of Obstetrics and Gynaecology, University of Edinburgh. The unit will be operated, as from August 1, under the direction of Dr R. V. Short who is at present Reader in Reproductive Biology in the Department of Veterinary Studies at Cambridge.

dertse (Rand Corporation, Santa Monica) described the application of a vertically integrated numerical model to study the circulation in Jamaica Bay, New York, which has a complex topography. A prediction of advective transport due to the influence of wind, using a three-dimensional numerical model of the Irish Sea, was described by Dr N. S. Heaps (Institute of Coastal Oceanography and Tides, Birkenhead). This work indicates that in this particular problem the boundary conditions, including the bottom topography, are far more important than the Coriolis effect.

A different treatment of an advective process was described by Dr W. D. Forrester (Bedford Institute of Oceanography), who has applied the condition of zero salt transport to determine the reference surface in geostrophic calculations of the flow in the St Lawrence estuary. The value calculated for the mean flow agrees remarkably well with that determined from run-off and other factors.

What Makes α -Helices?

IT is possible to make some generalizations about which amino-acids, and which kinds of sequences of amino-acids, tend to occur in α -helices in globular proteins. A new analysis, using information theory, is presented by Robson and Pain in next Wednesday's *Nature New Biology* (July 26). The chief object is to determine whether and to what extent the helix-making or helix-breaking tendency of a given residue in a sequence is directional; that is, whether it depends on the direction in which the sequence is read.

The analysis is based on a series of proteins of known sequence and structure. As a baseline Robson and Pain take proline, which sterically forbids α -helix formation on its N-terminal side. The following general rules emerge: alanine, leucine and isoleucine are helix-promoting in both directions; proline is helix-promoting on its C-terminal side; glycine, serine and especially glutamic acid favour helices on the C-terminal

side, and glutamic and aspartic acids both disfavour helices on the N-terminal side. Asparagine and glutamine are neutral. Lysine, and to a lesser extent histidine and arginine, tend to favour helices on the N-terminal side, whereas lysine, threonine and phenylalanine inhibit helix formation in the other direction. The remaining amino-acids are neutral in both directions.

The possible reasons for the polarity of the conformational effects of amino-acid residues are various. Charged side chains can form hydrogen bonds and could interact with the helix backbone dipole. Other residues with hydroxyl or amide groups can also hydrogen bond to backbone peptide groups, and in addition the most stable combinations, in van der Waals terms, of the backbone dihedral angles can also depend on whether the given side chain is on the N- or C-terminal side of the peptide bond in question.

Population Screening by the Cervical Smear

ARTHUR I. SPRIGGS

Laboratory of Clinical Cytology, Churchill Hospital, Oxford

Dr Spriggs makes a critical appraisal of the practice of testing for cancer of the cervix by means of cervical smears.

EVERY year, more than 1.5 million cervical smear tests are done in England and Wales¹. This massive population screening programme, promoted over the past seven years by the Department of Health and Social Security, aims to prevent cancer of the cervix uteri by discovering and removing localized precancerous lesions.

Cervical cancer accounts for about 1% of female deaths in this country. The disease almost always begins in a very limited area of the cervix, where columnar cells are replaced by squamous cells. At this point the columnar epithelium normally seems to have the ability to change its programme, and differentiate into metaplastic squamous epithelium. The whole of this cellular no-man's-land can be surgically removed ("conization") without necessarily interfering with the function of the cervix or with fertility or parturition. Cervical cancer is therefore unusual in that it affects an area which can be harmlessly removed, and which is accessible to direct inspection and to sampling by biopsy or simply by taking a smear with a blunt spatula and examining for abnormal cells. It would seem to offer a unique opportunity for cancer control, not by attacking the chain of causation (which is largely unknown) but by removing the offending tissue at a very early stage of development.

Screening by the vaginal or cervical smear for unsuspected precancerous conditions of the cervix was first introduced about twenty-five years ago. After worldwide use on a vast scale, its practical value in preventing deaths from cervical carcinoma has still not been clearly demonstrated. There are two quite separate uncertainties. First, the presumed "precancerous" lesions are very variable, and not enough is known about their spontaneous course if left untreated. Second, the epidemiological data might be expected to reveal a substantial effect if many lives are being saved, but the figures are equivocal. To maintain that no cancers are being prevented one would have to be sceptical to the point of perversity, but there is a reasonable doubt whether the massive effort is achieving all that was claimed for it and the propaganda required to bring women for screening rules out any possibility of a controlled trial.

The putative precancerous states which are discovered by the cervical smear test are, according to the terminology of the committee appointed by the Royal College of Obstetricians and Gynaecologists², as follows.

First, there is dysplasia, a spectrum of changes from minor irregularities in squamous metaplastic epithelium (mild dysplasia) up to a tissue with all the visible hallmarks of malignancy other than invasion; by definition, however, there must be some degree of maturation towards the surface.

The second detectable state is carcinoma *in situ*. This tendentious name is unfortunately too universal to be changed. It is applied to an epithelium which is undifferentiated throughout its thickness. It differs from anaplastic carcinoma in that no invasion is seen. Many, perhaps most, pathologists depart from the agreed definitions and use the term carcinoma *in situ* for lesions which, on grounds of cellular irregularity, give the impression that they are neoplastic whether they show surface maturation or not. The

distinction is drawn differently by different observers, and it is important to realize that the published statistics from different centres cannot therefore be meaningfully compared, nor are there any objective criteria which can be introduced in our present state of knowledge.

Third is microcarcinoma, a term recommended by the RCOG committee² for those cases of carcinoma *in situ* or severe dysplasia in which there are areas of incipient or dubious invasion of the subepithelial connective tissue. It is also known as "carcinoma *in situ* with minimal stromal invasion". Again, there are differences in interpretation which make comparison between different centres unreliable, particularly as the word "microcarcinoma" is sometimes used for a clinically occult but otherwise ordinary carcinoma (a condition which is also occasionally detected by the cervical smear).

Fortunately, there is no great difficulty in identifying the central group of conditions, comprising severe dysplasia and carcinoma *in situ*, and these are being discovered daily as a result of cervical smear tests, but little is yet known about their natural history.

The first inference that these conditions are precancerous came from their histological appearance. Cancer must begin somewhere, and these look like beginning cancers. Their histochemical features, their behaviour in tissue culture³, their chromosomal aberrations (including evidence of clonal proliferation⁴), all show a strong resemblance to invasive cancer. The same things are seen at the edges of invasive cancers; moreover, microcarcinoma appears to be the incipient (or abortive?) development of invasion out of the *in situ* stage. It would therefore be difficult indeed to think of any stronger *a priori* reasons than those we have already for supposing carcinoma *in situ* to be precancerous.

Direct attempts to establish the relationship have been both retrospective and prospective. Howard Jones and his colleagues at Baltimore⁵ searched the notes of known cases of cervical carcinoma in an attempt to find any whose cervix had been biopsied in the past. They found twenty-four such cases, and were able to review stored histological material going back as far as twenty years. All had been reported at a time when carcinoma *in situ* was not recognized as a precancerous condition. On review, seventeen had carcinoma *in situ* in the old biopsy sections; in eleven of these the interval between biopsy and clinical carcinoma was five years or more, and in six was more than ten years. This seems to demonstrate that cancer of the cervix is preceded as a rule by a long histologically recognizable precancerous stage. (Of course we do not know what proportion had invasive cancer in some other part of the cervix at the time of the initial biopsy.)

Of prospective studies, the largest are those of Petersen⁶ and Lange⁷, both from Copenhagen, together totalling 227 cases studied by biopsy during and after the Second World War, and followed without any other treatment. After ten years, about 25% had developed invasive cancer of the cervix, and further cancers continued to appear at even longer intervals, although the curve appears to flatten out between 30 and 40%. The chief objections to this evidence are, first, that the initial biopsy might have failed to reveal that invasive cancer was present already and, second, that the repeated biopsies may have removed some of the lesions piecemeal. To conclude that 70% of the lesions are harmless could therefore be either a gross overestimate or a gross underestimate. In studying the fate of histologically

abnormal tissue, one is constantly faced with the same almost insuperable difficulty, that the lesion has to be removed in order to make the diagnosis; if some is left behind, it may not be identical to the part which has been examined, and the smaller the biopsy the less reliable is the conclusion drawn from it.

It could be argued that, in this context, the presence or absence of a missed invasive focus is immaterial. If biopsy and histological examination had never been invented, the fact that this group of lesions, characterized by positive cervical smears, are frequently followed after an interval of several years by clinically obvious cancer would surely recommend this method for case finding at an early stage.

For some types of cancer, for instance that of the lung, it is suspected that "early" diagnosis has little effect on ultimate survival, but simply prolongs the time during which the patient knows that he has a fatal disease. This does not apply at all to carcinoma of the cervix. Most localized (stage I) cervical cancers presenting clinically are effectively cured, that is they do not recur after treatment and the individual finally dies of something else⁸. As for carcinoma *in situ* and microcarcinoma, I do not know of any reports of death from carcinoma of the cervix following normal treatment for these. The British Columbia workers report one case of metastatic carcinoma in the para-aortic lymph nodes among 3,893 cases of carcinoma *in situ* and microcarcinoma treated principally by simple hysterectomy or conization⁹.

It is certainly possible, even likely, that the cases being detected cytologically are chiefly those which, if left alone, would have had a slow growing and therefore curable form of cervical cancer. This is not universally true, as was shown in a recent small series¹⁰ of women with positive smears on routine examination who failed to have any further procedures, even a biopsy, for at least three years. Of thirteen cases, four developed invasive carcinoma and two of them died, an outcome which would have been most unexpected if treatment had been carried out at the occult invasive stage, and highly unlikely if it had been carried out while the lesion was still precancerous.

Up to this point, I have mostly presented material tending to favour screening of the symptom-free population by the cervical smear. It first became medically orthodox to advocate this in Britain about ten years ago, long after it was accepted in America. In 1962 an editorial in the *British Medical Journal*¹¹ stated that "these experiments are over, and the value of the screening method is accepted". At present, however, there is a swing of the pendulum towards scepticism, largely as a result of critical analysis of the statistics of large screening surveys.

The largest of the early surveys, that of Memphis and Shelby County, Tennessee¹², covering 150,000 women, showed that precancerous plus early invasive lesions could be discovered in about 0.5% of hitherto unscreened women; it also indicated that the occult or preclinical course of invasive cancer of the cervix lasted for three years (based on the ratio of prevalence to annual incidence of invasive cancer) and represented a valuable pickup of unsuspected disease. Data from the British Columbia programme¹³ showed that women who had never been tested displayed about eight times the incidence of overt invasive carcinoma, compared with women who had ever had a cervical smear, implying that this gave protection. It was not always appreciated by people who read and quoted this that the screened and unscreened groups were different self-selected populations with different ages and social backgrounds.

Once the incidence figures for carcinoma *in situ* became available¹⁴ (new disease arising in previous "negative" cases), it was possible to construct age-distribution curves for incidence and prevalence of the presumed stages of the disease. It was found that carcinoma *in situ* has its peak incidence at ages between twenty-five and thirty, and its

peak prevalence at thirty-five to forty, whereas invasive carcinoma was commonest at age fifty-five and later. The fact that the incidence curve for carcinoma *in situ* enclosed a much larger area than that of invasive carcinoma supported the idea that the former often fails to progress to cancer (or, perhaps, that it comes and goes repeatedly before progression). Ashley¹⁵ concluded from the existing figures that carcinoma of the cervix exists in two forms, a relatively slow and benign type in younger women, and a more rapidly growing type in older women. The latter accounted for most of the deaths. In a later critical analysis of the mass screening figures, Knox¹⁶ pointed out that the natural history of the disease could not, in fact, be inferred from the data at all, as "the information is simply not there". He also spelt out what further information would need to be collected in order to draw reliable conclusions—in particular he suggested annual smears on sufficiently large numbers of women in defined cohorts, and correction for false negative reports.

The existing incidence figures are certainly much inflated by the inclusion of "false negatives". The sequence of a negative smear followed by a positive may be due to the new development of disease, or to a failure of the first test to detect the lesion. In conditions of routine screening false negative reports are probably given in at least 10% of tests on women with carcinoma *in situ*, and it may be nearer to 20%. As a proportion of all "prevalent" disease this may not seem large, but these cases form a high proportion of negative→positive sequences, and seriously dilute the genuine new incidence of disease.

Another fact which makes the age-distribution curves difficult to interpret is the likelihood that women beginning their sexual activity in different periods of history have different expectations of contracting the disease. According to Adelstein's¹⁷ analysis of the age-specific death rates in England and Wales, the cohort of women who were young adults during the Second World War have shown an upward trend, possibly related to exposure to some sexually transmitted agent, while later cohorts showed a fall. Present levels of incidence of carcinoma *in situ* could be a reflexion of the "permissive society", but naturally women aged under thirty hardly appear yet in the cancer mortality tables.

The British Columbia data are at present being analysed in detail, and are awaited with great interest, as demonstrating the natural history of a human cancer from its incipient stages.

The object of cervical smear screening is, of course, to prevent deaths from carcinoma of the cervix, and the real test of its efficacy is to discover whether deaths are being prevented. According to Boyes¹⁸, about 75% of the 0.5 million adult women in the Province of British Columbia have had at least one smear test. If this degree of coverage is correct (and turnover of the population makes it difficult to assess), then one might look for a substantial fall in mortality from cancer of the cervix. In the imaginary situation of a fully effective preventive measure being suddenly applied to a random 75% of the population at risk, then there should be an almost immediate 75% fall in mortality, only delayed by cases already incurable at the time of application. In practice, there has been a fall from a mean annual death rate of 10.9 per 100,000 in the period 1959 to 1962 to a rate 7.1 per 100,000 in 1969 and 6.9 per 100,000 in 1970 (D. A. Boyes, personal communication). Even this moderate fall is unlikely to be due entirely to the screening programme, because the mortality has fluctuated in this way in previous decades, and because falls in mortality have also been occurring in other "developed" countries where screening has been much less intense¹⁹; moreover, the more recent rates would need to be standardized for age before it is accepted that they represent an important effect.

Opponents of screening are inclined to suggest that these

results are poor because the conditions being discovered are practically harmless and that fatal carcinomas are not preventable by this means. There is, however, a more plausible explanation. We know that invasive carcinoma is principally seen in women who have not been screened. Therefore, if the total death rate remains high, this cannot be attributed to failure of the technique or of its rationale, but simply to lack of participation in the preventive measure on the part of most of those at high risk. Also, the type of women who fail to come for a cytological test probably also fail to report symptoms until the disease is advanced, and therefore will contribute disproportionately to the mortality figures.

In England and Wales, the laboratory facilities and the trained technicians available would already be able to handle the load of five-yearly screening of all women over the age of thirty-five, which was the policy provisionally introduced in 1965. These facilities are in practice being used in a different way. Large numbers of women are having tests repeated at less than the five-year interval, which is widely thought to be too long. Also, nearly 50% of the smear tests are done on women under thirty-five, whose chance of dying of carcinoma of the cervix is small, while most women in the age groups where this disease is common have not yet been tested at all. The best lower age limit and the best interval between tests are both matters of current debate, and will depend as much on resources as on our concepts about the pathological process. Fig. 1 shows the age-specific death rates from carcinoma of the cervix in England and Wales, and this clearly shows the importance of using our resources on women over thirty-five, especially those who have not yet been tested. Many authorities consider that precancerous conditions ought also to be eliminated from women who are not yet at high risk, and that it should be part of official policy to test all women over thirty, or even twenty-five, especially as they can be "caught" at antenatal or family planning clinics. This is happening already. But is it reasonable to test girls of fifteen to twenty-five, a group with an age-specific death rate from carcinoma of the cervix of 1 per million per year, when there is also the attendant possibility of causing prolonged anxiety in those whose tests are not negative?

The medical profession does not like to price human life, and both doctors and the public probably feel that certain fatal diseases are so terrible that they should be prevented at whatever cost, if only the knowledge of how to do it is available. Even so, resources are not unlimited and some assessment has to be made of the return for money spent. A few years ago this approach was discussed by Pole²⁰. If it was assumed that one-third of the cases discovered would otherwise have progressed to overt cancer, with screening at four-yearly intervals, he estimated that the cost to the National Health Service would be about £2,000 for each life saved. If none of the lesions found represents a case of cancer effectively prevented, then the costs of screening, estimated at £1,200,000 per year, are altogether wasted. He did not mention the other extreme possibility, that all or most of the lesions develop into invasive cancer; this would bring the cost down to less than £1,000 per life.

To save manpower and money, it has often been suggested that automation would be the answer. To learn a moderate competence in "reading" cervical smears takes a technician about six months. To reproduce the screening process by mechanical or electronic scanning or sorting is possible in principle, but after some determined efforts there is still no effective instrument²¹. To search for wanted objects which vary among themselves, and differ only slightly from more numerous and similarly variable unwanted ones, is evidently just what the human eye and visual cortex have been evolved to do, and this performance will be difficult to match even with very expensive equipment. A partially automated marking system, by which

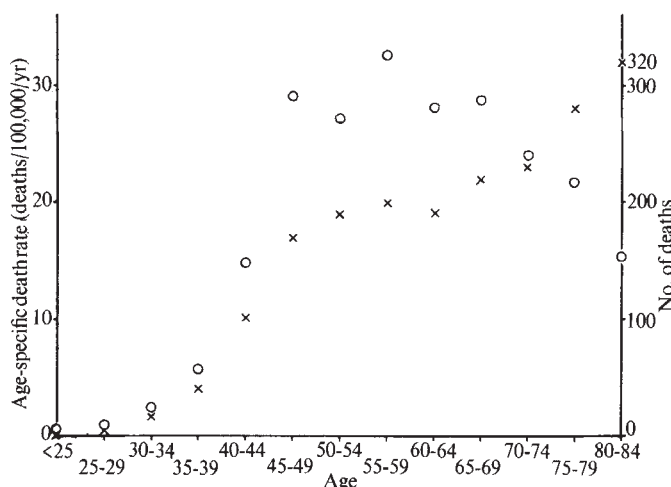


Fig. 1 O, Deaths from carcinoma of the cervix in England and Wales, 1969; x, age-specific death rate from carcinoma of the cervix, 1969. (From ref. 22.)

abnormal microscopic fields are selected for human viewing, seems to offer the best chance of cutting down the labour of screening, which at present takes several minutes a slide.

Doubts about the ratio of cost to benefit may be decisive in determining policy in other countries, but here the investment in manpower, equipment and training has been made already. More than 9,000 positive smears are being found every year. The reasons for expecting a preventive effect are so strong, and the disappointing results up to now are so easily explained, that there seems no choice but to press on and bring the test, if possible, to those at maximum risk—the older women in the lowest social classes—in whom the barrier of fear and misconception still remains to be broken down.

I thank Dr Max Wilson for helpful comments.

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High Energy Gamma Radiation from the Galactic Centre Region

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Balloon observations of gamma-ray sources near the galactic centre are described. These show good correlation with known X-ray sources. No diffuse emission was observed; gamma-rays apparently originate from point sources.

A SEARCH for high energy gamma radiation (>100 MeV) from the galactic centre region was carried out on a balloon flight from Palestine, Texas, on September 20, 1971. This entailed making observations at zenith angles of up to 50° . The balloon reached its ceiling at 2230 UT and floated at ~ 127 k foot until 0830 UT on September 21. The data presented here were obtained during the first two hours after reaching float altitude. The region of sky covered during this part of the flight (Fig. 1) includes the galactic equator between $5^\circ < l^{\text{II}} < 30^\circ$. We used the apparatus described earlier^{1,2}.

The output from each of the four counter telescopes could be combined logically in various ways to provide alternative angular acceptance profiles. For this flight we used a fan shaped pattern with the narrow dimension in zenith in order to minimize the contribution from the enhanced atmospheric background gamma radiation from the horizon. The track of each event in the spark chamber was recorded as a 90° stereo pair image on 35 mm film together with a digital display giving the outputs of a two axis gimbal-mounted magnetometer, the zenith angle and the time to within ± 1 ms. We classified the events according to simple visual criteria. Only pairs and straight single tracks were used in the analysis; there were 794 pairs and 676 single tracks. Another 430 events were probably induced by neutral particles but produced a significantly scattered single track and we attribute a further 228 events to charged particle leakage, albedo electrons and neutrons. The celestial coordinates of the point of origin of each event were calculated from the track direction and telescope orientation. This information was stored in a model sky array of equal solid angle bins, each subtending $1^\circ \times 1^\circ$ at the celestial equator. We found the angular response function of the telescope by generating a 24×40 array of 1° square bins in θ and ϕ , the angles to the telescope axis in each of the two orthogonal views. This array was smoothed and normalized before being used to calculate the effective exposure time for each sky bin and corrections were applied to compensate for the zenith angle variation in the atmospheric background.

As a first step in the analysis of the data, we determined the relative exposure of different parts of the sky by summing the number of photons within an $11^\circ \times 11^\circ$ array (approximately equal to the FWHM of the telescope) which was moved in 1° steps to cover the whole of the region of sky observed. Any point sources present would have a much smaller angular extent than this array and, unless very intense, must have relatively little effect on the exposure time calculated. In order to search for

point sources the data were also summed into a $5^\circ \times 5^\circ$ array of similar bins. For each of these bins we deduced an expected number of gamma rays from the atmosphere using the exposure time; this was compared with the observed number. In three of the bins the observed number exceeded the expected number of gamma rays by more than about 3σ . Each of these regions includes a known X-ray source. These areas of high gamma ray emission and all the Uhuru X-ray sources³ which lie in the region are indicated in Fig. 1.

These preliminary results were verified using the absolute exposure time calculated from the angular response function and the live time between events. We divided the sky array into a series of regions with approximately the same exposure, and derived a distribution of the number of gamma rays in each bin, excluding the regions containing possible sources. Each distribution is a good fit to a Poisson distribution. We calculated the mean of each and plotted them against exposure time (Fig. 2). The best fit straight line through these points gives the expected number of gamma rays from the background in each bin. These results agree well with those obtained by the preliminary method. A list of possible sources together with their probable identification is given in Table 1.

The source strengths have been calculated using the atmospheric background flux⁴. The value $\phi_B = 1.0 \times 10^{-3} \text{ cm}^{-2} \text{ s}^{-1} \text{ sr}^{-1} \text{ mb}^{-1}$ has been used and we deduced the point source strengths from the relation

$$\phi_S = N_S \omega \phi_B / N_B$$

where N_B is the number of gamma rays expected from the background, N_S is the number of gamma rays observed from the source, ω is the solid angle subtended by the bin, and

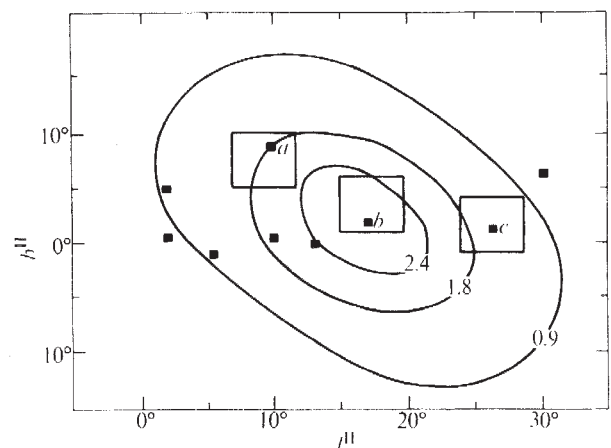


Fig. 1 Region of sky observed. Exposure value contours in units of $10^6 \text{ cm}^2 \text{ s}$. The black squares show the position of known X-ray sources and the open squares indicate the regions of anomalously high gamma ray emission. a, 2ASE 1728-16; b, 2ASE 1813-14; c, 2ASE 1833-5.

Table 1 Possible Sources Observed on September 20–21, 1971

No.	l^{II}	b^{II}	No. observed	No. expected	Poisson probability	Equivalent sigma	Point source strength $\times 10^{-5} \text{ cm}^{-2} \text{ s}^{-1}$	Possible identification	l^{II}	b^{II}
1	26.5	+1.5	29	16 ± 1.3	0.001	3.3	2.9 ± 0.8	2ASE 1833–5 (ref. 3)	26.4	+1.0
2	17.5	+3.5	50	33 ± 2.6	0.003	3.0	1.8 ± 0.4	SER XR-2 (ref. 9) GX 17+2 (ref. 10) 2ASE 1813–14 (ref. 3)	17.5 16.6 16.4	+2.0 +1.5 +1.3
3	9.5	+6.5	35	22 ± 1.6	0.005	2.8	2.1 ± 0.6	GX 9+9 (ref. 10)	8.9	+8.8
3*	9.5	+6.0	19	8 ± 0.6	0.0004	3.6		2ASE 1728–16 (ref. 3)	8.5	+9.0

* Using a $3^\circ \times 3^\circ$ bin.

ϕ_B is the atmospheric background intensity. The effective atmospheric depth of the spark chamber, including the effects of the gondola, was 4.5 mbar when observing the zenith.

In a search for diffuse radiation from the galactic plane we summed the observed and expected numbers of photons in 1° bins of constant galactic latitude b^{II} over the range $5^\circ < l^{\text{II}} < 30^\circ$ (Fig. 3). Although there are peaks coincident with the latitude of the reported sources, no significant excess is observed within $\pm 3^\circ$ of the galactic equator when the contributions from these sources are removed. Over this region a total of 152 gammas was observed. The expected number for the same area is 154, so 2σ excess would imply an observation of 179 gammas. We are therefore able to set a 95% confidence upper limit to the line source strength along the galactic equator at

$$\phi_G < 8 \times 10^{-5} \text{ cm}^{-2} \text{ s}^{-1} \text{ rad}^{-1}$$

If the sources that we report were observed using a telescope with low resolving power they would contribute an apparent line emission of $\phi_G = 1.5 \times 10^{-4} \text{ cm}^{-2} \text{ s}^{-1} \text{ rad}^{-1}$ which is in good agreement with the value obtained by Fichtel⁵ and the corrected value reported by Clark *et al.*⁶ with OSO III.

Frye⁷ has made three balloon flights which have covered part of the region observed by this flight but he has not reported any sources coincident with those reported here. This may be because the sources lie very close to the 50% exposure boundary for two of his flights. The sources which were reported by Frye are at too low an elevation to have been observed by our flight from Palestine. Fichtel⁵ has also examined this region and reported no point sources although the observed line source intensity of $(2.0 \pm 0.6) \times 10^{-4} \text{ cm}^{-2} \text{ s}^{-1} \text{ rad}^{-1}$, which is incon-

sistent with the upper limits set by Frye⁸ and by ourselves, is consistent with the value which would be obtained if the sources found by us were unresolved by Fichtel.

The energy of the observed gamma rays was determined from measurements of the scattering of the electron tracks in the spark chamber. When combined with a Monte Carlo calculation of the telescope efficiency as a function of energy, these results yielded a value for the atmospheric background intensity which is in good agreement with that obtained by others. These results will be described fully later.

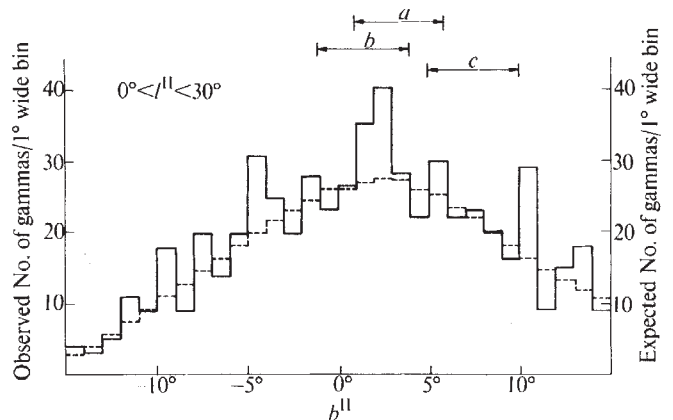


Fig. 3 Observed number of gamma rays and expected number of gamma rays in 1° wide strips summed over $5^\circ < l^{\text{II}} < 30^\circ$. —, Gammas observed; ----, gammas expected. a, 2ASE 1813–14; b, 2ASE 1833–5; c, 2ASE 1728–16.

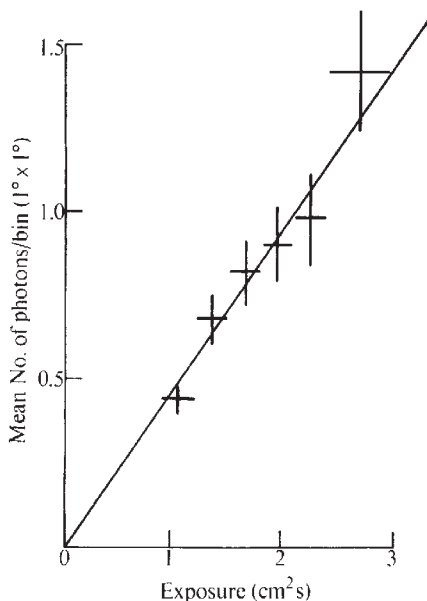


Fig. 2 Plot showing the mean number of atmospheric gamma rays per $1^\circ \times 1^\circ$ bin as a function of the exposure.

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Servo Action in Human Voluntary Movement

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Muscular movements are under the control of a servo similar in many ways to those used in engineering control systems but with a subtlety of design not found in man-made servo mechanisms—including an automatic gain compensation for altered load which must be useful, for example, for adjusting to reduced *g* on the Moon.

If in the course of a voluntary movement we meet with an unexpected obstruction we soon exert our muscles harder to overcome it. The question is, how soon? If an ordinary voluntary reaction time is involved the delay is not likely to be much under a seventh of a second (140 ms). On the servo theory of muscle control, however, the delay ought to be much less. This theory^{1,2} supposes that the contraction of the main muscle is driven by contraction of specialized sensory structures in the muscle, the muscle spindles. The sensory endings on the spindles function as misalignment detectors and automatically turn on more contraction, via the stretch reflex arc, if the rate of shortening of the main muscle falls behind the shortening of the spindles. This type of follow-up servo action, akin to power-assisted steering on a motor car, would tend to make the main muscle shorten at the same rate as the spindles. If an obstruction were met with, the delay in turning on more contraction to overcome it would be only the brief delay associated with the operation of the stretch reflex.

So far the evidence for the servo theory from animal experiments has been equivocal^{3,4}, and there has been no convincing evidence for its operation in the human subject. In the present experiments, direct evidence has been obtained by interfering unexpectedly with flexion movements of the top joint of the human thumb.

This movement was chosen because it involves only one muscle, the flexor pollicis longus, which lies in the forearm. The proximal phalanx was held in a clamp so that the axis of rotation of the top joint coincided with the axis of a low-inertia electric motor (Printed Motors Limited, Type G9M4, used as a torque motor moving a fraction of a turn only). The spindle of this motor carried at one end a potentiometer, to record thumb position, and, at the other, an arm against which the pad of the thumb pressed to move or be moved by the motor. This arm incorporated a strain gauge for measuring the force exerted by the thumb. All the phenomena to be described can be seen on force records, but they are more elegantly demonstrated by using, as an index of the activity of the flexor muscle, its action potentials (electromyogram) led off by a pair of surface electrodes over the belly of the muscle in the forearm and then amplified and integrated. The slope of the integrated record gives the degree of contraction of the muscle.

There was a standing current in the motor which held the motor back against a stop and thus defined the starting position of the thumb. The subject made flexion movements in his own

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time, about once in 5 s. To standardize the movements he was given a tracking task on a cathode ray tube. By keeping two spots together he executed a 20° movement in 1.2 s. To smooth out irregularities several records were averaged in a 'Biomac' (Data Laboratories Limited).

All movements were begun against the constant force offered by the standing current in the motor, but about half way through perturbations were sometimes introduced. The sweep of the 'Biomac' was triggered at approximately 8° of flexion, and 50 ms later one of four things happened unpredictably, as determined by the output of a randomizing device: either the motor current did not change (a "control" trial); or it dropped rapidly to a fraction of its previous value and remained there for the rest of the movement, allowing the thumb to accelerate ("release"); or it rapidly increased to roughly double, applying a step of extra force to the thumb and driving it back ("stretch"); or finally (by feedback from the potentiometer on the spindle) the motor from then on was caused to simulate a spring, so that further movement was met with an increasing opposing force. The rate of the spring was such as to double the force in 3°. When it met the spring the thumb was almost arrested (a "halt" trial), but was not driven back.

The 'Biomac' sweep lasted 250 ms. From 50 ms to the end of the 'Biomac' sweep the subject's spot on the tracking cathode ray tube was extinguished, so that he had no visual clue as to what was being done to his thumb. In an experiment, the subject went on making trial movements until sixteen (or sometimes eight) of each kind, as they turned up at random, had been accumulated for averaging in the appropriate 'Biomac' channel.

The type of result obtained with the two authors (C. D. M. and P. A. M.) who acted as subjects is shown in Fig. 1a. The lower part gives the records of mechanical displacement and shows the average for the "control" trials, with the "release", "stretch" and "halt" records diverging from it after 50 ms. The electrical records above show that after a delay of about 60 ms the muscle attempts to compensate for these deviations from the desired track by reacting in the opposite sense. In the other subject, C. D. M., whose arm length is 12% less, the figure is more like 50 ms. These latencies are only a fraction of the shortest recognized voluntary reaction times, and they were the same in earlier experiments⁵ in which the subject was faced with two rather than four choices at the 50 ms mark. Voluntary reaction times increase rapidly with the number of choices (Hick's law⁶); but here the latency is independent of the number of choices.

It seems safe to conclude that the response to stretch is reflex and we proceed on the assumption (later to be questioned) that it corresponds to the muscle-spindle-excited stretch reflex of decerebrate experimental animals. Our latencies for the stretch reflex agree sufficiently with those found in the human elbow flexor by Hammond⁷. As far as we are aware there are no figures available for the latency of the stretch reflex, as opposed to the tendon jerk, in animals. The fact that the halted and release responses have the same latency as the stretch reflex makes it likely that they are manifestations of the same mechanism. If this is accepted, then the release response is the negative of the stretch reflex and it demonstrates that the muscle must have been receiving excitation *via* the stretch reflex arc at the moment of release. (This argument is essentially the same as the original argument from the silent period

which led to the servo theory¹.) The response to halting is, in effect, a stretch reflex without muscle stretch. It is the best piece of evidence we have for the original servo theory because, from the animal evidence, it is difficult to see how it could arise except by contraction of the spindles stretching the sense endings on them. And a surprisingly brisk contraction it must be, for (in this experiment, but not always) the slope of the "halt" response approaches that of the "stretch" response. This is even more conspicuous in Fig. 2a, to which we shall come later.

The sensitivity, too, of the system as revealed in the "halt" trials is remarkable. From the geometry of the tendon and thumb joint, the rate of tracking, the minimum time that must be lost in conduction in the reflex arc *via* the spinal cord and the latency of the servo response, it can be calculated that the misalignment signal calling for more contraction must have left the muscle when its degree of shortening was only some 50 μm (0.05 mm) less than it would have been if the muscle had gone on shortening unimpeded. And this figure is an upper limit which assumes that movement of the thumb stops at once when the extra resistance begins to develop, that the muscle does not continue to shorten against the various compliances in series with it, and that the stretch reflex is spinal. In the release trials, the misalignments which turn the muscle completely off must be of the same order of magnitude. The detection, within milliseconds, of these minute misalignments in an actively shortening muscle many centimetres long represents a considerable feat of sensory discrimination and we begin to see why muscles require the profuse and elaborate sensory apparatus they have long been known to possess and which has always hitherto been something of a mystery.

Returning to the consideration of Fig. 1a, as already noted, the response to stretch is not very much steeper than the response to halting, although, particularly in the early stages, the tracking error and, hence, the misalignment presented to the muscle spindles is several times greater during stretch. This

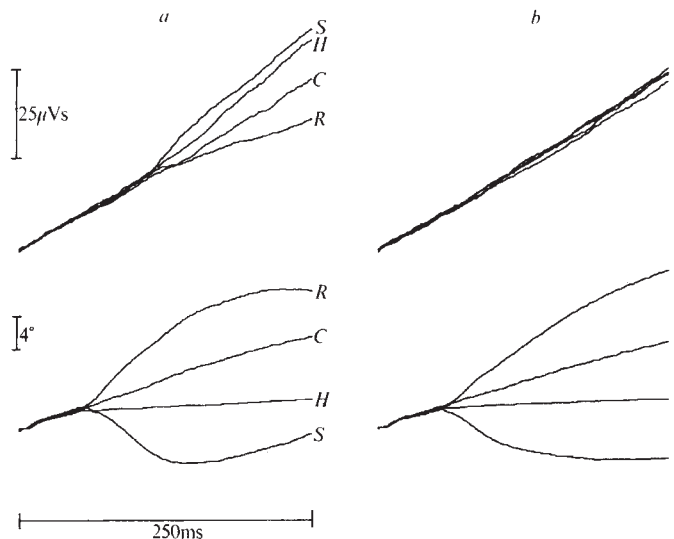


Fig. 2 As Fig. 1, but with the movements against a ten times greater initial resistance. Subject P. A. M.; an experiment on a different day from Fig. 1.

suggests that the spindle-based excitatory machinery is beginning to saturate, although the degree of contraction reached in these experiments, even in the stretch responses, can easily be shown to be only a small fraction (roughly 5%) of what the muscle can achieve.

The release trials, on the other hand, tend to emphasize the importance of the servo machinery: other experiments, in which action potentials were not integrated, showed that release could completely silence the muscle, with the usual brief latency. Merton's experiments⁸ on the "silent period" during steady contractions in the human subject indicate that this is likely to be true at all levels of contraction up to maximal, suggesting that the saturation level of the servo machinery must be raised as the level of contraction rises, presumably by something akin to a change of loop gain.

This is not the only possibility. The theory of α - γ coactivation⁹, which, in various forms, has been widely favoured^{3,4,10}, proposed that some excitation reached the muscle *via* the servo loop (the γ route) while some by-passed the servo loop and played directly on the main motoneurons (the α route). This theory has recently been greatly strengthened by the important direct human evidence of Vallbo¹¹. One way in which large contractions could be obtained on this theory would be by increasing the α component after the γ route begins to saturate, without changing the loop gain. But in this case it should be more difficult with large contractions to silence the muscle by release, and the extra contraction turned on by stretch or halting should become a smaller proportion of the total.

To decide between these two mechanisms, experiments were performed in which the initial resistance offered to movement was increased ten-fold, with alterations in the forces during release and stretch so as to produce approximately the same displacements as before. (An initial resistance of this value requires roughly one quarter of the maximum force the long flexor can exert to overcome it.) The results of these experiments were unequivocal. At the high force the electrical activity of the muscle was much increased and the recording gain had to be reduced. In both subjects the shape of the electrical responses remained remarkably similar to those seen at the lower level of force. A typical record is shown in Fig. 2a. The response of the muscle to release, stretch or halt is given by the change in slope of the integrated electromyogram, so the general similarity of Figs. 1a and 2a shows that the *proportional* change in the degree of activation of the muscle in the release, stretch and particularly the halt trials remains effectively constant over this ten-fold change in initial force. Hence the muscle activation turned on by a given misalignment (the gain) is proportional to the initial force.

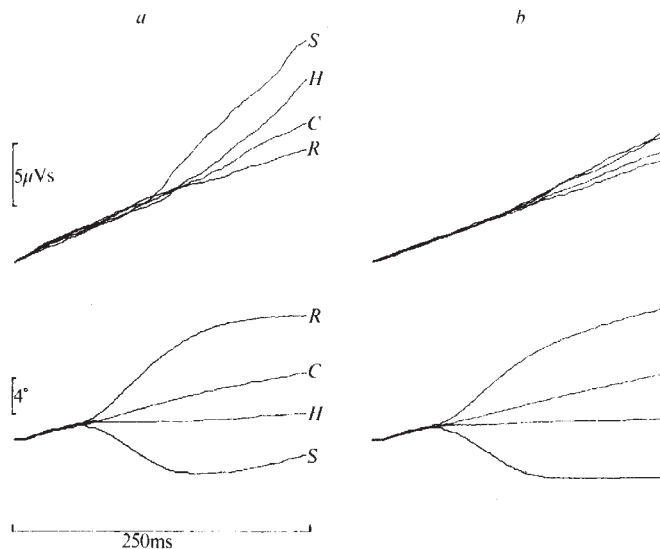


Fig. 1 Servo-type responses from the muscle flexing the top joint of the thumb. During the course of a tracking movement against an initially constant resistance, as described in the text, the movement may either be reversed (S) eliciting a stretch reflex, or halted (H), or allowed to accelerate by a reduction of the opposing resistance (R). In the control trials (C) none of these things happen. The initial resistance was a torque of 150 g cm (about 2% of the maximum torque that the subject could exert). The top records are the integrated electromyogram of the flexor muscle, the slope of the trace giving the degree of activation of the muscle. The bottom records give the angular position of the terminal phalanx of the thumb. Each trace is the average of sixteen trials, formed in a 'Biomac' averaging computer. a, Records taken with a normal thumb; b, records taken in the same experiment after anaesthesia of the thumb induced by occluding the blood supply for 1.5 h with a cuff at the wrist. Subject P. A. M.

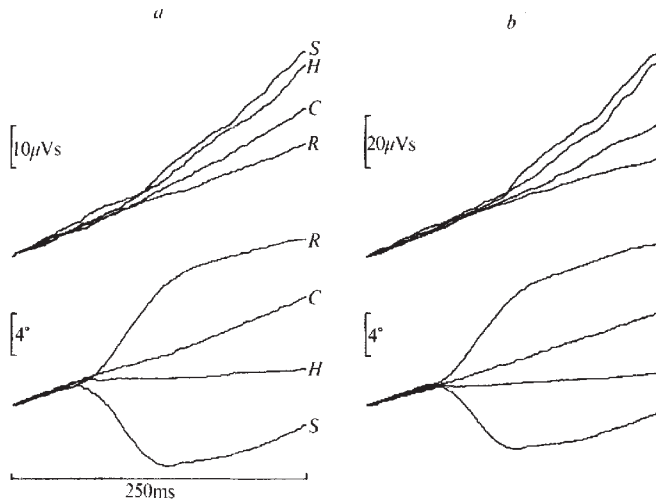


Fig. 3 Gain compensation during fatigue. The initial force in this experiment was low, the same as for Fig. 1. *a*, Fresh muscle. The muscle was then fatigued by applying maximal shocks to the median nerve at the elbow at 50 s^{-1} for 60 s. Recovery was prevented by a blood pressure cuff on the upper arm, arresting the circulation. *b*, Muscle fatigued. The electrical responses are of the same form as before fatigue, but scaled up by a factor of roughly 2, as shown by the calibrations. Force records (not illustrated) showed that the forces developed in the halt and in the other responses were the same as before fatigue. In these experiments each trace is the average of eight trials. The period of circulatory arrest was too short to cause ischaemic nerve block. Subject P. A. M.

According to Professor P. H. Hammond, whom we have consulted as a practising control engineer, change of gain with load is not a feature of man-made servo systems. Evolutionary pressures have produced a more flexible device than have engineering requirements. If an engineer designed an artificial arm, a powered prosthesis, with which one could wind up one's car to start the engine, incorporating conventional servo assistance to get over the compression strokes, and then used it to wind up a clock instead, it would break the mainspring when it came to the end!

One possible mechanism for the gain control in the servo loop postulates an input to the servo which, as the demanded force alters, has the function of altering the number of α motoneurons that are sensitive to spindle excitation, in proportion. A demand for increased force would be met (in whole or in part) by increasing the number of motoneurons responding to spindle input in proportion (or at a slower rate if the larger motor units are recruited later). Loop gain would automatically increase in proportion, as the number of active motoneurons increased. It is known that the number of α motoneurons active does increase with force and that all α motoneurons receive a spindle input. We propose that the spindle input does not lead to excitation of an α motoneuron unless the gain input is active at the same time—and *vice versa*.

To illustrate this proposal, imagine a motor car in which the mean speed for a journey was determined by altering the number of cylinders (representing motoneurons) in use. To keep the speed constant during the journey the accelerator could be depressed to climb a hill, or released when descending. The briskness of response to the accelerator (the gain available) would be proportional to the number of cylinders in use, and hence to the initial speed.

An important attraction of the idea of an input to the servo that causes a motoneuron to become accessible (or to become more accessible) to spindle excitation is that it would provide a "focusing" effect, permitting the higher centres to use servo action for discrete contractions of one small part of a large muscle, despite the known fact that excitation from a single spindle is often very widely distributed among the motoneurons of a large composite muscle, or to the motoneurons of more than one muscle. The need for such a "focusing"

action in movements of individual fingers using the common flexor and extensor muscles in the forearm has been emphasized by Phillips⁴.

At one time, for reasons which will emerge presently, we entertained the notion that signals from pressure receptors in the thumb itself were responsible for sensing the force exerted and turning up the gain appropriately¹², but this theory was made implausible by the behaviour of the servo during muscular fatigue. The muscle was fatigued by working it while the circulation was occluded by a blood pressure cuff on the upper arm. In the fatigued state the contractility of the muscle is lowered and it has to be more strongly activated to achieve the same force. This shows up as an increase in the electrical activity, which, as with increased load, entails a reduction in the recording gain. The force and displacement records were little altered as contractility fell, but the electrical responses were scaled up in the same way that they are scaled up when the demanded force is raised (Fig. 3). It seems therefore that muscular fatigue is compensated for by an increase of gain elsewhere in the servo of the same type as occurs with increased load. Because in the fatigue experiment the pressures on the thumb are unchanged, cutaneous receptors cannot be controlling the mechanism that boosts the gain.

Automatic compensation for load and fatigue have always been numbered among the supposed advantages of the muscle servo but the original theory¹ did not predict that the compensation would take the form or show the effectiveness that it does. Even at that time, however, it was noted that, contrary to expectation, when skilled finger actions, such as writing or playing musical instruments, are carried out during circulatory arrest, there is little falling off in performance almost until the muscles become so weak that they are unable to execute the necessary movements at all¹³. This now becomes intelligible.

Early on in these experiments we made a puzzling discovery which does not seem to have any correlate in the animal literature and which may cast light from an entirely new direction on the whole scene. If the thumb is anaesthetized, without interfering in any way with the muscle itself in the forearm, servo action is lost and the stretch reflex depressed⁵. The thumb may be anaesthetized either by a ring block with 'Xylocaine', or by a rubber band round the base of the proximal phalanx left on for 1.5 h or more, or by inflating a narrow cuff around the wrist for a similar period. We have done numerous experiments of this type on both subjects at low forces, always with a similar result (Fig. 1*b*); and we have confirmed that the same occurs in a fatigued muscle and at high forces (Fig. 2*b*). All the mechanical records are, in their first half, closely similar to those made before anaesthesia, but the responses in the electrical record are all greatly depressed throughout. Towards the end of the record, the mechanical responses in both Fig. 1*b* and Fig. 2*b* demonstrate the effects of the lack of servo compensation, by their wider or more persistent divergence from the control record.

An unexpected subjective observation of interest is that both subjects report that it needs more conscious effort to start the movement when the thumb is anaesthetic, particularly to restart it after it has been halted, and especially with the first few movements of a freshly anaesthetized thumb. Thus anaesthesia of the thumb provides both objective and subjective evidence of the advantage to the subject of servo action in his muscles.

Our experience is that anaesthesia depresses all the responses simultaneously at both high and low forces. Apart from providing further confirmation for the view that the stretch, halt and release responses share a common mechanism, this suggests that anaesthesia acts by turning down the gain of the servo loop, for if, on the alternative view, anaesthesia put the servo out of action by stopping spindle contraction, one would expect the release response to be lost first, followed by the halt response, the stretch reflex disappearing last. Whichever is the case, movements of an anaesthetic thumb must be produced by

the α route. The records in Figs. 1*b* and 2*b* indeed display in an extreme form the characteristics described above (in considering α - γ coactivation) for movements against a large resistance when the extra force was to be produced by increasing the α component without turning up the γ loop gain, that is, a reduction in that part of the contraction which is sensitive to stretch, halt, or release. (From another point of view the results can be regarded as establishing in the human subject, albeit with an anaesthetic thumb, the original thesis of Granit, Holmgren and Merton⁹ that the same movement can use the α and γ routes in varying proportions.)

It might be held that all the responses in Figs. 1*a* and 2*a* are directly due to receptors in the pad of the thumb sensitive to the force to which it is subjected. But the fatigue experiments suggest that such receptors are unlikely to be involved in the gain control mechanism, and we have evidence that they are not necessary for the responses to stretch or halt, because normal responses of this kind are obtained when the thumb moves the motor by pulling on a string cemented to the thumb-nail. The phenomenon of the silent period⁸, in which a rise of force is associated with a complete cessation of muscle activation, is also evidence against this possibility. In animals, of course, stretch reflexes are obtained in isolated muscles with the rest of the limb denervated.

What, then, is to be made of this effect of peripheral anaesthesia? The evidence cited earlier has shown that increasing activation of the servo, whether to overcome an extra load or offset fatigue, automatically boosts the gain (possibly by rendering more motoneurons susceptible to spindle excitation), and as a consequence servo action is focused on the muscle needed for the movement. We now learn that sensation in the thumb itself is necessary for that part of servo activation which turns up gain and focuses spindle excitation, but not, apparently, for that part which causes the spindles to contract. This power of thumb sensibility over the gain and focus control might be exerted either at spinal or at cerebral level. The latter possibility seems the more attractive. It could mean, for example, that the cerebral cortex cannot throw into play a mechanism to focus spindle excitation on to the thumb flexor if, because it is anaesthetic and not under visual control, attention cannot be focused on the thumb.

This is the time to recall Phillips's suggestion⁴ that the stretch reflex may not (as hitherto implied here) be purely spinal but may involve what he calls a transcortical loop. In the baboon, and presumably in man, signals from muscle spindles reach the cerebral cortex¹⁴, so that our conditional focusing may be an action on cortical rather than spinal motoneurons. A transcortical stretch reflex has not been clearly established in animals or in healthy human subjects, but something of the kind, with a latency similar to the latency we have found for the stretch reflex in healthy subjects, is seen in rare cases of myoclonic epilepsy. In Carmichael's case¹⁵, investigated electrophysiologically by Dawson¹⁶, myoclonic jerks could be elicited by stretch of muscle and only by that variety of mechanical stimulus. The pathological findings in this case were predominantly cerebellar degeneration (J. G. Greenfield, unpublished post-mortem report, the National Hospital, Queen Square). In this patient electrical stimulation of the ulnar nerve at the wrist evoked a large potential wave in the contralateral motor area 3 cm in front of the central sulcus (the position of which was verified at post-mortem) and, therefore, clearly in front of the area in which evoked responses to sensory stimulation are found in healthy subjects. It was followed by a generalized myoclonic jerk, but the latency of this jerk in the arm muscles was not recorded. Such measurements have, however, been made on other myoclonics by Fullerton and Giblin (reported by Halliday¹⁷), by Lance and Adams¹⁸ and by Kugelberg and Widén¹⁹. In all these cases the latency of the myoclonic jerk was roughly double the latency of the evoked cortical wave. This would give a jerk latency of some 50 ms for the forearm muscles, agreeing with our healthy stretch reflex latency. The cortical origin of these

myoclonic jerks was perhaps established most definitely in Kugelberg's and Widén's case¹⁹, in which they were limited to one leg and were cured by excision of a small region of the leg area of the opposite motor cortex.

Transcortical stretch reflexes are thus very much on the cards. Jumping ahead of the evidence for the sake of a definite proposal to serve as a basis for further experiment, suppose that in a voluntary movement of the thumb cortical motoneurons connecting to both α and γ spinal motoneurons are activated. If tactile sensibility in the thumb is active, signals from muscle spindles in the thumb flexor arriving back at the cerebral cortex are given access to the α cortical motoneurons, thus completing a servo loop. The extent of access determines gain. If the thumb is anaesthetic, access is barred. A movement can still be made, involving, as usual, activation of both α and γ cortical motoneurons, but it requires greater effort, of which the subject is aware. Although the spindles will contract, they cannot thereby give servo assistance, because the feedback pathway to the cortical α motoneurons is not open—at any rate in the experimental situation with which we are at present dealing, in which visual clues to the perturbations introduced are excluded, and there are no auditory clues. This scheme explains all our present results, but assigns no role to the spinal stretch reflex, although the existence of tendon jerks in healthy subjects, of a latency consistent only with a spinal reflex arc, proves that the spinal stretch reflex is competent to act in ordinary life.

Quite independently, however, of such interpretations in terms of specific receptor mechanisms, we are thus making five new experimental points: (1) that there is servo action, sensitive, brisk and so early as clearly to be automatic, in voluntary movements of the thumb, (2) that the gain of the servo loop is proportional to the force exerted, (3) that the gain of the servo loop is automatically compensated against contractile fatigue in the muscle, (4) that the latency of servo action is the same as the latency of the stretch reflex, and (5) that both servo action and the stretch reflex are heavily dependent on sensation in the thumb itself, as opposed to the muscle that moves it. The relevance of these findings to the interpretation of spastic and other pathological states of muscle in man will not escape notice.

Finally, while making acknowledgment to the Department of Trade and Industry, who, in part, financed the work with some such return in mind, it is appropriate to observe that whereas the servo theory of muscular contraction arose from the application of engineering ideas to physiology, it looks as if nature may be about to repay the compliment and reveal some novel mechanisms for control engineers to reflect upon.

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LETTERS TO NATURE

PHYSICAL SCIENCES

On the Nature of the Tycho X-ray Source

OF the five X-ray sources which are identified with remnants of supernovae, the Tycho 1572 source is of particular interest. In this case the X-ray emission cannot be considered as the continuation of the synchrotron radio spectrum because it can easily be shown that, independent of the mechanism of injection, the spectrum must be "bent" in the frequency region $\nu < 10^{13}$ Hz. Also, it cannot be assumed that the observed X-radiation is thermal and caused by hot plasma behind the front of shock-wave produced by the expanding envelope of a remnant. This mechanism qualitatively explains X-radiation from Cassiopeia A if the undisturbed density n_0 of interstellar matter in the vicinity of the explosion is about 30 cm^{-3} . This value of n_0 is in excellent agreement with the density of the HII region which is observed around Cas A (ref. 1). But in the case of the Tycho remnant one must assume that $n_0 \sim 5 \text{ cm}^{-3}$ if the radiation is thermal. Such a value of n_0 contradicts the observed large dimensions of this remnant, which, according to all indications, has exploded in a relatively rare medium between the clouds of interstellar matter, where $n_0 \leq 0.1 \text{ cm}^{-3}$. This excludes the possibility of explaining X-radiation from Tycho as thermal radiation from hot plasma.

It seems probable that this source should be identified with a young pulsar which originated after the explosion of the Tycho supernova. Because of "unfavourable" orientation of the rotation axis of this pulsar, coherent radio emission is not observed.

But there are good reasons to believe that young pulsars should generate synchrotron radiation in the optic and X-ray ranges (similar to NP 0532, ref. 2). The power of this radiation must be a very steeply diminishing function of the pulsar's age. It is essential to note that the intensity of synchrotron radiation of NP 0532 between pulses is not zero. For example, according to Vishvanathan³, the intensity of radiation between the main and secondary "peaks" is about 1.5% of the maximum intensity in the main "peak". According to Bradt *et al.*⁴, in the X-ray range the "interpulse" intensity is near 10%. In the 100–400 keV range this intensity is sufficiently larger (I. Kurfess, unpublished work). Consequently, one should remember that there is a "quasi-isotropic" component in the X-radiation of young pulsars. The time-averaged power of this component is at least equal to the "pulse" component. The X-ray flux from the Tycho supernova remnant is ~ 25 times smaller than that from the Crab Nebula⁵ and, consequently, it is half the X-ray flux from NP 0532. Since the distance to SN Tycho is approximately 2.5 times that to the Crab, the observed X-radiation from the Tycho remnant can be explained if the power from the expected pulsar, which is situated inside Tycho, is three times that from NP 0532. This can be explained naturally by the youth of Tycho's pulsar. Recently Henriksen *et al.* (unpublished work) suggested that X-radiation from Tycho and some other sources can be interpreted as thermal radiation of his crust heated due to dissipation of rotation energy of a neutron star. In our case it should be supposed that the crust temperature is $25 \times 10^6 \text{ K}$. But in

this case the linear dimensions of the source must be unacceptably small—above 1 km.

The observable tests of our hypothesis are as follows: (a) measurement of angular dimensions of Tycho's X-ray source—according to our hypothesis, the upper limit of angular dimensions of this source must be essentially smaller than those of the radio source; (b) discovery of a small periodic modulation of X-ray flux from Tycho caused by expected anisotropy of radiation of Tycho's pulsar; (c) a study of 18th to 19th magnitude stars in the central part of the Tycho radio source with the object of discovering an optical pulsar with periodically modulated flux; (d) discovery of a "point" X-ray source in the remnant of Kepler's Supernovae 1604.

The "quasi-isotropic" component of pulsars' synchrotron radiation must play an essential role in the physics of the Crab Nebula. Evidently, this radiation generated by relativistic electrons closed in the radiation belts of NP 0532. The spectrum of this radiation is essentially harder than in the main pulse. This can explain the expected relation between pulsars and nebular synchrotron spectra².

It should be noted that in connexion with Pacini's explanation of "glitch" in NP 0532, the systematic observation of "quasi-isotropic" component synchrotronous radiation of NP 0532 is desirable.

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Lunar Electrical Conductivity

SONETT *et al.*^{1,2} have inverted sunward lunar surface magnetometer data to obtain a lunar electrical conductivity profile, using the poloidal magnetic response to a spatially uniform source field of a radially structured conducting sphere immersed in an infinitely conducting plasma^{3,4}. The experimentally determined lunar response expressed as the tangential magnetic spectral amplification factor is shown in Fig. 1 together with the best fit poloidal responses for a two-layer and a multi-layer Moon and their corresponding electrical conductivity profiles⁵.

The spatial symmetry imposed on the boundary conditions by this model of the interplanetary magnetic field–Moon interaction neglects the solar wind plasma–Moon–void geometry and the finite application time of the interplanetary magnetic field which result from the solar wind flow past the Moon. We have studied qualitatively the effects of including these boundary condition asymmetries through numerical examinations of an asymmetric cylindrical model of the interaction (Fig. 2). In our model a cold, infinitely conducting

solar wind plasma is incident with velocity $v_0 \hat{x}$ and the solar wind borne magnetic field $\mathbf{H}$ is aligned along the axis $\hat{z}$ of a cylindrical Moon⁶.

Fig. 3 shows the numerically determined sunward surface response of the asymmetric model of the interaction for a core-crust conductivity model with a highly resistive thin outer layer added to eliminate the toroidal mode. The analytically determined cylindrical analogue of the poloidal response of the symmetric model⁶ is also shown. Comparison reveals,

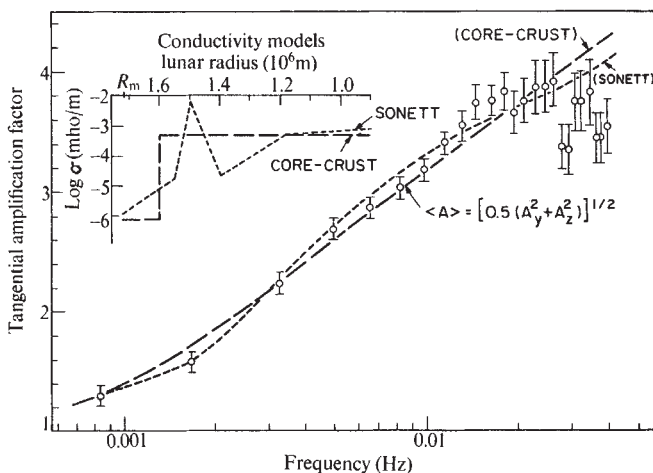


Fig. 1 Experimental tangential amplification factor from Sonett *et al.*², shown with the calculated poloidal responses for the inset conductivity profiles reproduced in part from ref. 5.

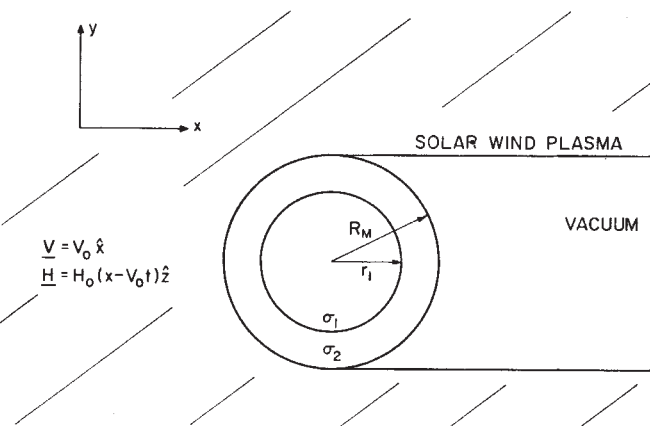


Fig. 2 Asymmetric model of solar wind borne magnetic field interaction with cylindrical Moon.

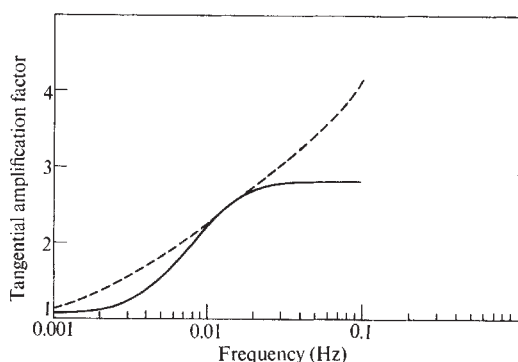


Fig. 3 Cylindrical analogue of poloidal response. ---, Symmetric analytical; —, asymmetric numerical, $v_0 = 3.0 \times 10^5$ m/s; $r_1 = 1.4 \times 10^6$ m; $\sigma_1 = 5.0 \times 10^{-4}$ mho/m; $\sigma_2 = 1.5 \times 10^{-6}$ mho/m.

first, the depressed asymmetric response at low frequencies resulting from diffusion of field lines around the core into the anti-solar cavity on a time scale $\mu_0 \sigma_2 L^2$, where $L \sim R_m$ is the scale length of the diffusion process; and second, the flattened asymmetric response for high frequencies which results from application of the incident field to the sunward lunar surface on a time scale of R_m/v_0 .

These features of the response of the asymmetric model are also present in the experimentally determined response (Fig. 1). An attempt to fit these features using the poloidal response of the symmetric model of the interaction resulted in the complicated conductivity profile obtained by Sonett *et al.* We also note that the response of the asymmetric model is insensitive to increases in the core conductivity σ_1 , from which we conclude that the experimental sunward tangential magnetic response does not exclude a more conductive lunar interior.

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Lunar Electrical Conductivity—Reply

REISZ *et al.*¹ consider, in the preceding letter, two conceptually important points regarding the lunar transfer function inversions which we reported^{2,3}. That work used a symmetric confining current theory so that the dark hemisphere diamagnetic cavity effect was ignored, as we pointed out at that time; Blank and Sill⁴ estimated that the effect upon the sunward hemisphere transfer function is small. Recently Schubert and Lee (private communication) have computed the fields associated with a magnetostatic configuration where confining currents exist sunward of the Moon, upon the surface of a perfectly conducting core and upon the walls of the diamagnetic cavity. Their results are applicable here by relating their core radius to an effective skin depth at a specified frequency. Approximate damping depths are given in ref. 3. For frequency $f \lesssim 0.001$ Hz and $R_c \sim 0.6 R_m$ where R_c is the core radius and R_m the lunar radius, the cavity correction to front side data not adjacent to the terminator is about 4%. For $f \gtrsim 0.01$ Hz the correction increases to about 20%. The effect upon conductivity is trivial for $R_c \sim 0.6 R_m$ and is a factor of about 3 for $f \gtrsim 0.01$ Hz; the resultant change in estimated deep temperature is insignificant. For the shell, dominated by the higher frequencies, a combined change in shell depth and conductivity takes place but is beyond the scope of this letter. So we do not agree that field line diffusion through the crust and past the core can account for the very large difference in transfer function in Fig. 3 of ref. 1 for $0.002 \lesssim f \lesssim 0.006$. We note also that the skin depth at $f \approx 0.002$ Hz for the core conductivity¹ indicates a core radius of only 900 km, hardly sufficient to produce the effects described. Lastly, the difference between the two cases shown in Fig. 3 of ref. 1 is non-monotonic, which does not seem likely for various reasons. For example, higher harmonic effects ($l > 1$) are unimportant below $f \sim 0.008$ Hz (Fig. 1). On the basis of

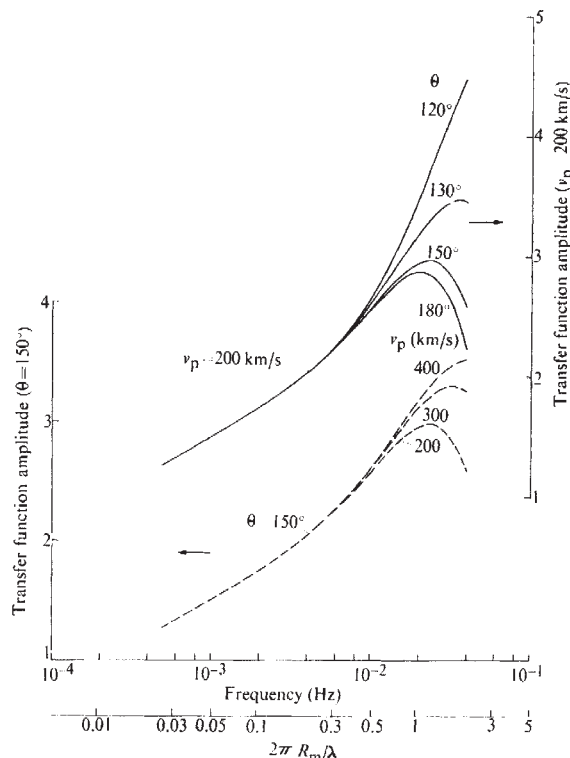


Fig. 1 Idealized transfer function behaviour showing effect of varying phase velocity, v_p , and central angle between magnetometer and k . Lower scale demonstrated that the Moon lies in the Mie scattering domain⁵.

field line diffusion the fractional decrease in transfer function should increase with frequency.

Unfortunately, the correct assertion by Reisz *et al.* concerning the "finite application time of the interplanetary magnetic field", which we take to mean excitation by higher order magnetic multipoles, is clouded by the limitations of the cylindrical geometry which they employ, their lack of knowledge of the angular spectrum of the incident wave field k vectors, and the relative geometry of the surface magnetometer and k , all of which are needed to define correctly the higher order excitation⁵⁻⁷. We agree that the higher orders ($l > 1$) can flatten out the transfer function and indeed turn it over for appropriate value phase velocity and position of the magnetometer with respect to k . But Reisz *et al.* seem to be unaware of our calculations which include higher order multipoles and which also assess the source of the transfer function asymmetry, surface generated noise, and higher order multipoles, all of which conspire to complicate the final inversion⁵. Nevertheless it can be stated with some confidence that errors well in excess of one order in conductivity would be required to increase the deep temperature estimates substantially, because these are determined by the dominant dipolar ($l=1$) excitation at low frequency and are thus free from higher order effects, and our cavity calculations show field line sweeping to be unimportant at low frequency. Further confidence in this is obtained by noting the correspondence between our determination and the transient analysis in the lunar cavity⁸. Temperature estimates could be raised substantially by decreasing the fayalite mole fraction to below 2% in a test olivine⁹, but this seems contrived.

Our earlier report of a non-monotonic conductivity is not unique but is a member of a set of possible profiles when ($l > 1$) magnetic excitation is included in the problem. Geometry effects upon idealized transfer functions are shown in Fig. 1 and indicate very strong multipole effects. Model solutions are shown in Fig. 2 using the best data available at present (from Apollo 12, ref. 5). Fig. 3 gives some forward calculated transfer functions fitted to the A_{min} which is the

data corrected for noise. Although this work is still in progress, we think that the effect of the cavity will be to move the outer edge of the shell to a radius perhaps 50 km greater with little conductivity change.

Lastly, we wish to point out a common misconception regarding the theoretical treatment. Blank and Sill⁴ treated the low frequency or large wavelength (Rayleigh) limit, that is

$$\frac{2\pi R_m}{\lambda} \ll 1$$

Schubert and Schwartz, on the other hand, provided a complete

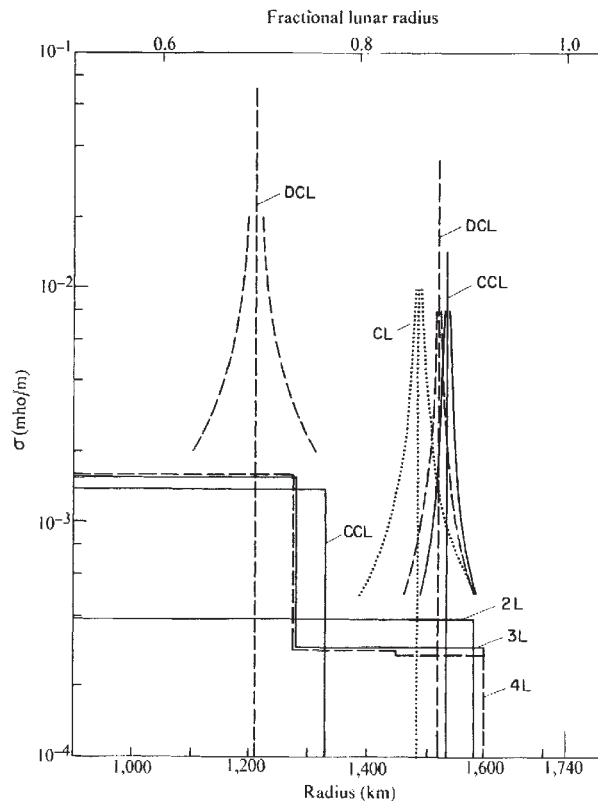


Fig. 2 Bulk conductivity models for two layer (2L), three layer (3L), four layer (4L), current layer (CL), double current layer (DCL), and core plus current layer (CCL). All models are iterative using noise corrected A_p , using phase velocity $v_p = 200$ km s⁻¹, and angle between magnetometer and K measured from the centre of the Moon of 150°. The hyperbolae define current layers for which $\delta\sigma = \text{constant}$. (For further details and restrictions, see ref. 5.)

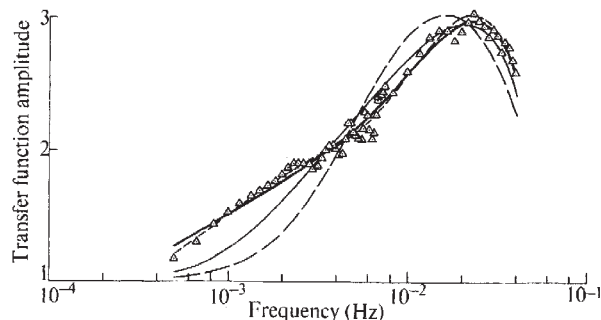


Fig. 3 Forward calculation of transfer function amplitude corresponding to selected models of Fig. 1. 3L, 4L, and CCL models are too close to one another to show on this scale. —, 3L, 4L and CCL ($\epsilon^2 = 0.29$); ---, DCL ($\epsilon^2 = 0.28$); ···, 2L ($\epsilon^2 = 1.34$); - · -, CL ($\epsilon^2 = 4.08$). Δ , Experimental A_{min} . The ϵ^2 are the sum of the square of the standard deviations of the means; all models are reasonable fits with the exception of 2L and CL (Sonett *et al.*⁵).

classical partial wave analysis^{6,7}, though both theories used a symmetrical confining current layer. Our work has generally been based upon the Schubert and Schwartz treatment of the induction, which in turn has yielded the basis for analysis of the various orders of magnetic multipole encountered in the Mie regime.

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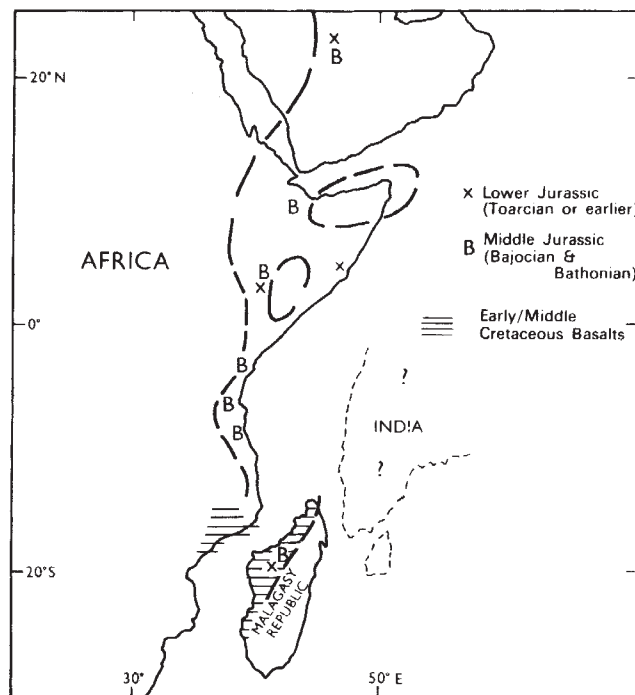


Fig. 1 Lower and Middle Jurassic seaways of Eastern Africa. Madagascar is shown nearer Africa, in line with the hypothesis of Green³. The contemporary position of India is not known, and is indicated only diagrammatically.

Mesozoic History of the East Coast of Africa

SEVERAL recent contributions on the history of the Indian Ocean and eastern coast of Africa¹⁻⁴ can be supplemented from other sources of information. Contrary to a general view which still persists⁴, the East African coast must have originated long before the postulated Cretaceous movements, for there is abundant evidence that a Mesozoic sea invaded the modern coastal area of Somalia, Kenya, Tanzania and Madagascar at least as early as Middle Jurassic, the dating varying within modest limits from place to place⁵⁻⁷. The Jurassic sea (Fig. 1) transgressed locally across pre-existing faulted troughs filled with continental Karroo sediments; in coastal Tanzania one internal rift already contained 10,000 foot of halite which had accumulated chiefly through the Trias⁶. This is the first symptom of the oceanic connexion, although the Permian rifting marks the initial tensional breakdown of the continental margin. The marine regime continued from the Jurassic to the present day without important interruption. Facies changes and overlap features from the Middle Jurassic onwards are consistent with this marine phase in Kenya and Tanzania forming an east-facing oceanic margin, either the Indian Ocean or its precursor.

Formerly, evidence of a particularly characteristic Lower Jurassic (Toarcian) fauna which was known in Arabia, NE Kenya and Madagascar, and Middle Jurassic fauna (Bajocian and Bathonian) identified in British Somaliland, coastal Kenya, Tanzania and Madagascar⁸, led to a belief that the marine invasion of the African coast crossed the horn of Africa from the north. On this basis the Indian Ocean coast of Somalia could have been a later development. The concept must be

modified, however, in the light of thick Jurassic beneath thick Cretaceous in this coastal belt. Lower Cretaceous measuring 6,000 to 7,000 foot in thickness is reported up to 100 km inland; Jurassic rocks are known to be very thick near Mogadiscio and Obbia, the latter deposits including 6,800 foot of chiefly Middle and Lower Jurassic in limestone facies, the deepest beds dated being Pliensbachian (Lower Lias).

It seems, therefore, that coastal Southern Somalia was occupied by an abnormally rapidly subsiding shelf in the Jurassic, the belt of subsidence migrating inland during the early Cretaceous. These features are consistent with progressive stretching of the crust as continental parting developed from early Jurassic onwards. There is no information available as to whether this vertical movement was related to contemporaneous faulting.

The early marine connexion could well have followed the African coast south from this area to Madagascar in its present position. The seaway would have been shortened if that island had been farther north, but the dating of the various Middle Jurassic and later Mesozoic beds in the 300 miles southwards from Mombasa gives no support to a progressive southerly transgression along the coast; the marine invasion seems essentially contemporaneous, as though from the present ocean.

The postulated southward displacement of the Madagascar micro-continent into its present position is one of the more crucial problems; it has always seemed strangely inconsistent with the contemporary northward travel of India during the same breakup of Gondwanaland. The stratigraphical evidence is equivocal, but with increasing knowledge of the East African coastal succession the oft-quoted fit against Kenya has seemed progressively more improbable.

Green³ has discussed the physical evidence of palaeo-latitude and suggests that Madagascar moved a moderate distance to the east of north, but not southwards, during the Mesozoic. His thesis is supported by the presence of very thick early Cretaceous volcanics in coastal Mozambique, together with extensive basalt flows in the Middle Cretaceous (Cenomanian-Turonian) of Western Madagascar⁹, which is consistent with the postulate of an opening minor plate junction in the Mozambique channel. Madagascar and Mozambique are unique in this region in their thick developments of volcanic rocks, which

with their near contemporaneity provide independent circumstantial evidence of direct palaeo-geographical relationship.

The north-south seafloor lineations which Veevers¹ thought symptomatic of late longitudinal drift are not clearly different from other north-south structural features which are known on the African coast and offshore⁶; some at least of these represent vertical (tensional) movements dating back to the Karroo and are pre-Middle or pre-Upper Jurassic.

The greatest crustal adjustments of the East African mainland coast are dated as Karroo—partly contemporaneous with Karroo deposition, and continuing into the earliest Jurassic—when normal faults exceeding 20,000 foot developed⁷. In the Middle Jurassic a stable continental margin regime supervened, and it is logical to think of the principal features of the Indian Ocean coast as established by that time. Other periods of faulting followed on the mainland, but the size of these did not approach that of the later Karroo movements. Madagascar has a similar history of fault movement. In the Tanzanian coastal belt the faults show a tendency to develop further seawards with passage of time⁷, showing that the reconstruction of Sowerbutts⁴ is, for this area, an over-simplification. There is no evidence of crustal instability on a scale which would presumably be associated with southward movement of an adjoining micro-continent in the post-Jurassic period. The contemporaneity of the later movements and associated transgressions of East Africa with incidents on a world wide scale had led to a concept of control by variation in water loading⁷, derived independently by Bott and Dean from stress analysis data¹⁰.

In summary, tensional conditions in the East African marginal area developed in the Permian. Salt water—presumably from a marine connexion—was flooding in by the Trias. A large part of the east coast of Africa in its present form appears to have been blocked out by the early Jurassic, and from the Middle Jurassic onwards this had the characteristics of a stable shelf fronting a sea or ocean. This might have been the triangular gap shown by Veevers *et al.* (Fig. 4 of ref. 1) but could equally well have been the early Indian Ocean; one or other is required. Later changes involved building out the shelf by thick sediments of Jurassic to late Tertiary date accompanied by limited faulting, but there are no indications of further major geographical adjustments.

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Isolation and Characterization of Stanols from the Green River Shale

We have recently reported the isolation of a triterpenoid alcohol, tetrahymanol, from the Green River Shale (60 × 10⁶ yr old)¹ together with a complex mixture of unidentified polycyclic alcohols. Further investigation of this mixture has revealed

the presence of a series of stanols and saturated triterpenoid alcohols in the carbon number range C₂₇–C₃₀. We now report the characterization of several of the stanols from this extract.

The sediment (1,000 g) was pulverized and extracted as before¹. We carried out silica gel column chromatography using heptane and mixtures of heptane and ethyl acetate (5 to 20% in heptane v/v). Appropriate fractions were purified by preparative thin-layer chromatography (TLC) as trimethylsilyl (TMS) ethers^{1,2}, and we analysed the purified TMS ether fractions by gas-liquid chromatography (GLC) on the liquid phases OV-101, JXR and OV-17. Retention indices were determined and separation factors calculated for some authentic stanols and compared to those found for the extract. Further analysis by GC-MS ('Dupont 21-492-1') using a packed capillary column (1% OV-101 on 'Gas Chrom Q', 26 foot × 0.03 inch glass column) gave the total ion current (TIC) chromatogram shown in Fig. 1. The vertical lines in the diagram represent the points at which mass spectra (70 eV) were recorded and the data obtained indicate the presence of isomeric ergostanols and stigmastanols. The mass spectral fragmentation patterns of stanol TMS ethers are characterized by ions at *m/e* 75, 215, 216, 217, 230 and 305 together with the appropriate molecular ion (M), M-15, M-90 and M-105 ions³. Table 1 gives the retention indices of peaks 1–10 of Fig. 1 and indicates the molecular ion or ions obtained by scanning through the peak. The chromatographic peaks corresponding to stigmastanols are characterized by ions at *m/e* 488; 473 (M-15); 398 (M-90) and 383 (M-105), together with the ions cited above as being common to all stanol TMS ethers. Similarly, peaks corresponding to ergostanols have ions of *m/e* 474, 459, 384 and 369. Fig. 2 shows line diagrams of the mass spectra obtained from peak 5 (a) and from peak 7 (b) in Fig. 1. The chromatographic and mass spectral data obtained for peak 7 were identical to those for authentic 5 α -stigmastanol ((24R)-24-ethyl-5 α -cholestan-3 β -ol obtained by catalytic hydrogenation of β -sitosterol) TMS ether.

Table 1 GC-MS Data from a Trimethylsilylated Green River Shale Alcohol Fraction

Peak No.	I* OV-101	Molecular ions (TMS)	Possible structure
1	2,925	—	
2	3,095	458	C ₂₇ -triterpenoid
3	3,160	474, 488	5 β -campestanol or 5 β -ergostanol
4	3,190	474, 488	C ₂₉ -stanol
5	3,235	474, 488	C ₂₈ and C ₂₉ -stanols
6	3,270	488	5 α -campestanol or 5 α -ergostanol
7	3,320	488	5 β -stigmastanol
8	3,365	—	C ₂₉ -stanol
9	3,385	500	5 α -stigmastanol
10	3,490	500	Pentacyclic triterpenoid
			Tetrahymanol

* 26 foot × 0.03 inch silanized glass column packed with 1% OV-101 on 80–100 mesh 'Gas Chrom Q' at 235° C.

Peak 5 has a similar retention time to both authentic 5 α -ergostanol ((24S)-24-methyl-5 α -cholestan-3 β -ol obtained by catalytic hydrogenation of brassicasterol) and 5 α -campestanol ((24R)-24-methyl-5 α -cholestan-3 β -ol obtained by catalytic hydrogenation of campesterol) TMS ethers which were not separable under these conditions. Examination of the mass spectra derived from these two compounds showed that their fragmentation patterns were very similar to each other and to that shown in Fig. 2 (a). It is, however, obvious from this latter mass spectrum that peak 5 also contains a stigmastanol. Calculation of the 5 α /5 β GLC separation factor from 5 α - and 5 β -cholestanol, two readily available reference compounds, shows that peak 5 corresponds in retention time to 5 β -stig-

Fig. 1 Part of a total ion current chromatogram derived from a purified Green River Shale "sterol" fraction (in the form of trimethylsilyl ethers). Chromatography was carried out on a 26 foot $\times$ 0.03 inch silanized glass column packed with 1% OV-101 on 80-100 mesh 'Gas Chrom Q' at 235° C.

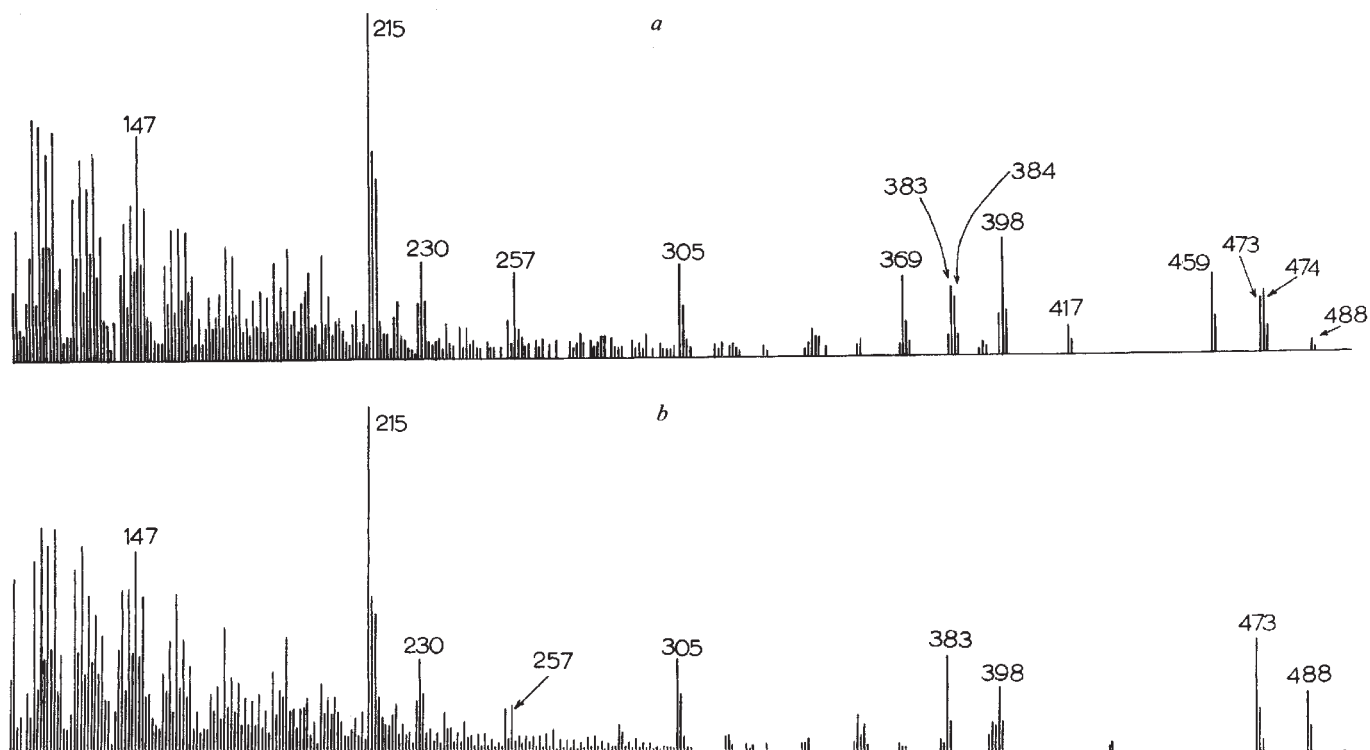
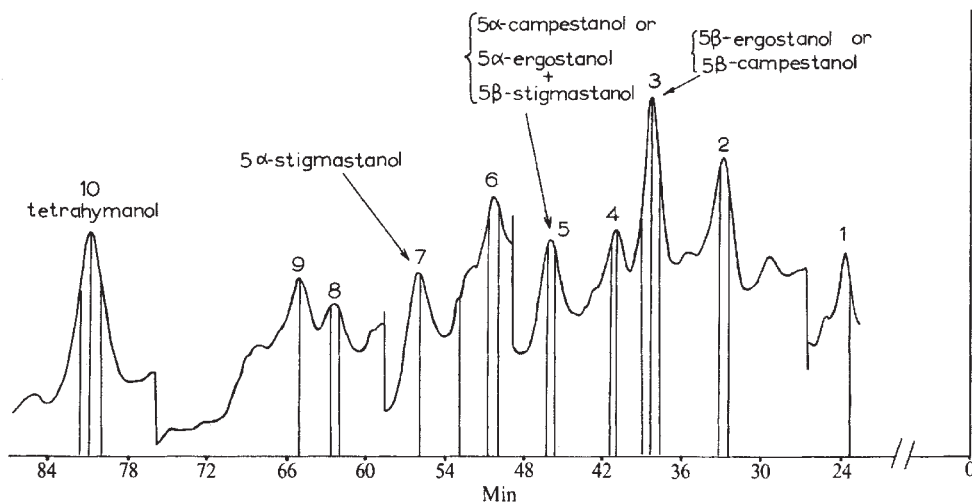


Fig. 2 Normalized line diagrams of the mass spectra of trimethylsilyl ethers of (a) a mixture of 5 α -ergostanol and 5 β -stigmastanol, and (b) 5 α -stigmastanol, obtained by GC-MS of a purified fraction from the Green River Shale. The spectra were recorded at 70 eV and normalized on the most abundant ion over m/e 110.

mastanol TMS ether. From the same calculation, peak 3 contains the TMS ethers of 5 β -ergostanol or 5 β -campestanol or a mixture of both. Mass spectral evidence shows that peaks 4 and 6 contain stanols and we are elucidating their structures.

Although stanols have been shown to occur in *Sphagnum* moss⁴ and in a pollen mixture⁵ they are extremely rare in the rest of the contemporary plant kingdom. This suggests that the stanols found in the Green River Shale result predominantly from the reduction of unsaturated sterols after deposition. The 5 α - and 5 β -C₂₈ and C₂₉ stanols now identified probably represent intermediates between the original Δ^5 -sterols and the previously identified 5 α - and 5 β -steranes from this sediment⁷⁻⁹.

Other components in the complex mixture illustrated in Fig. 1 are triterpenoid alcohols (C₂₇-30, structures under investigation), possibly the analogues of previously identified triterpanes⁷⁻⁹. Other investigations of a series of Recent sediments (Mono Lake, California)^{2,6,10} have shown the presence of 5 β -stanols and tetrahymanol (our unpublished

results) in sediments less than 12×10^4 yr old. These transformations can therefore happen early in the history of the sediment. It is hoped that investigations of the reduction of unsaturated sterols in a contemporary sedimentary environment will allow elucidation of the mechanisms of geological transformations.

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Adsorption of Ammonium and Some Primary *n*-Alkylammonium Cations by Soil Allophane

ALLOPHANE, an amorphous aluminosilicate mineral, is a major constituent of the clay fraction of soils derived from volcanic ash. The adsorption of inorganic cations by allophane depends on the solution concentration¹⁻⁴, the pH of the system^{2,3,5}, and the effective size of the cation^{4,6}. In view of the potential of allophane as a cheap and effective sorbent of organic wastes, for example, meat works⁷ and dairy effluents, surprisingly little is known about the mechanisms underlying the interaction of allophane with organic compounds. I report here some results of a study on the adsorption of ammonium salts and a homologous series of primary *n*-alkylammonium cations from dilute aqueous solutions by an allophane separated from the subsoil of Egmont brown silt loam (andesitic ash)⁸. To minimize possible interference from associated organic matter the soil was repeatedly treated with a hot dilute (6%) solution of hydrogen peroxide⁹. The $<2 \times 10^{-6}$ m equivalent spherical diameter fraction was obtained by dispersing the soil at pH 3 with an ultrasonic vibrator, sedimenting under gravity, flocculating the suspension at pH 6, washing with water, and drying the material at 35° C. The separated allophane has a carbon content of 0.9% and a silica/alumina ratio of 0.81. Adsorption isotherms were determined by the equilibrium method in which weighed amounts of the dry mineral were shaken overnight at 20° C with aqueous solutions of ammonium and the appropriate alkylammonium chloride of varying strength¹⁰. After centrifugation the concentration of ammonium and alkylammonium ions, hydrogen and chloride ions in the equilibrium solutions was determined and the amount adsorbed was estimated by difference.

All the isotherms belong to the "C"-class¹¹, the amount adsorbed increasing linearly with concentration up to a certain saturation value beyond which there is an abrupt change to zero slope (Fig. 1). Nearly equivalent amounts of chloride ions were taken up concomitantly, the range of pH values (5.8–6.4) of the equilibrium solutions being close to the measured isoelectric pH of the mineral⁵. Fig. 1 also shows that the adsorption of ammonium and *n*-alkylammonium ions by allophane can be reversed by lowering the solution concentration with the possible exception of the amount represented by the ordinate intercept.

These observations indicate that physical adsorption is the dominant process which may be expressed in terms of a partition of solute between the bulk and the interstitial water¹¹. Some non-physical or coulombic adsorption also occurred as revealed by the isotherms failing to pass through the origin^{2,6}. If Kitagawa's¹² model is adopted in which micro-aggregates of allophane are composed of close-packed spherical particles of $\sim 55 \times 10^{-10}$ m diameter surrounded by a monolayer of water molecules, the volume of this interstitial water at near saturation (97% relative humidity) is calculated as $\sim 15.5 \times 10^{-5}$ m³/kg. The physical adsorption of ammonium and its primary *n*-alkyl derivatives can then be represented by the equilibrium¹³



for which the equilibrium constant, K_a , is

$$K_a = \frac{(\text{RNH}_3^+)_{\text{interstitial}}}{(\text{RNH}_3^+)_{\text{bulk}}} \cdot \frac{\gamma_{\text{interstitial}}}{\gamma_{\text{bulk}}} = K_s \cdot K_\gamma$$

where K_s is the selectivity (partition) coefficient. The ratio of $\gamma_{\text{interstitial}}/\gamma_{\text{bulk}}$ may be replaced by that of the mean activity coefficients, $\gamma_{\pm}$, of the respective chloride salts. Since for dilute solutions the ratio of $\gamma_{\pm \text{interstitial}}/\gamma_{\pm \text{bulk}}$ does not significantly deviate from unity $K_a \sim K_s$, and

$$-\Delta G = RT \ln K_s$$

the linear relationship between $-\Delta G$ and alkyl chain length (Fig. 2) is similar to that observed for the exchange adsorption of these cations by synthetic near-faujasite¹⁵. It appears that the ease with which ammonium and *n*-alkylammonium ions can find vacant sites in the interstitial pores of the allophane micro-aggregates is inversely related to ionic size. This suggests that steric factors are important. As the size of the cation increases it becomes more difficult to pack the ions in the available pore space. Alternatively, the adsorbed cations block access to the interstitial pores causing a sudden decrease in available sites as indicated by the abrupt change of slope of the isotherms (Fig. 1). The existence of a plateau, however, does not necessarily imply that no fresh sites could be created¹¹. Indeed, the uptake of inorganic ions by allophane shows an overall linear increase up to high (~ 2 M) salt concentrations^{2,6}. It seems probable that there is a series of linear isotherms of the type shown in Fig. 1 if the concentration were to be increased in small step-wise increments beyond the present range.

The pH of many soils containing allophane lies between

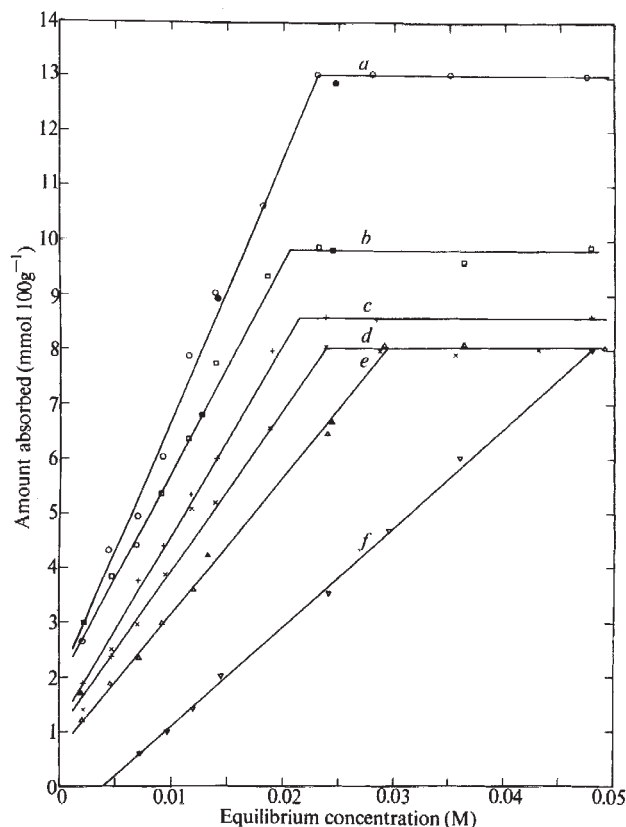


Fig. 1 Isotherms for the adsorption of ammonium and some primary *n*-alkylammonium cations by allophane at 20° C. The filled-in symbols represent desorption points. *a*, Ammonium (NH₄); *b*, methylammonium (Me₁); *c*, ethylammonium (Et₁); *d*, *n*-propylammonium (Pr₁); *e*, *n*-butylammonium (Bu₁); *f*, *n*-hexylammonium (Hx₁).

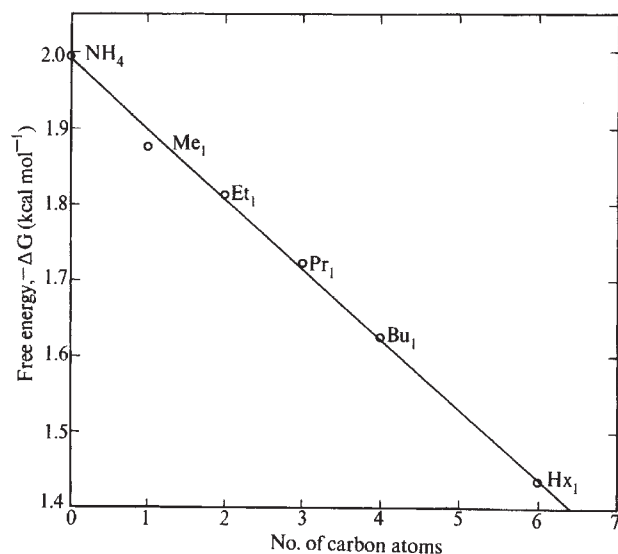


Fig. 2 Relation between the free energy change of adsorption and the number of carbon atoms in the alkyl chain.

5 and 6.5. Although small charged organic species may be adsorbed to an appreciable extent by such soils, they are not likely to be held strongly. This has important implications in the retention and release of cationic organic herbicides in allophanic soils. Using a range of soils, Knight and Tomlinson¹⁶ have reported that adsorbed paraquat (1:1'-dimethyl 4:4'-dipyridylum dichloride) is more readily displaced by a 0.05 M calcium chloride solution from soils containing mainly allophane than from soils in which the principal clay minerals present are of the crystalline layer structure type. The present results also indicate the possibility of using allophane minerals from soil as molecular sieve adsorbents.

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BIOLOGICAL SCIENCES

Immunogenic Effects of Foreign Materials on Plasma Proteins

THE increasing variety of polymeric materials considered for long term implantation in man has emphasized the importance of adequate testing for compatibility. Methods currently used

for evaluation¹⁻³, however, reveal little about the mechanisms which might cause incompatibility after prolonged implantation.

We have investigated another aspect of compatibility which considers whether long term implantation of certain materials may lead to toxicity through immunological mechanisms. Bases for these investigations lay in observations⁴⁻⁶ that materials immersed in plasma acquired at least a monomolecular layer of protein which was subtly denatured. Such denaturation enhances the immunogenicity of heterologous proteins in rabbits⁷. If autologous protein were adsorbed and denatured by materials implanted in a major route of blood flow, they might present a constant antigenic stimulus with development of antibodies to the adsorbed protein coat or to small amounts of desorbed, denatured protein released into the circulation. Certain materials might be considered to have undesirably intense immunogenic properties to the extent that alteration of the surface stereochemistry during adsorption might expose greater numbers of antigenic sites in autologous proteins; these would thus be unsuitable for implantation^{8,9}.

We first exposed plasma samples from individual rabbits to large surface areas of test material contained in polyvinyl chloride blood-storage bags. After exposure, the plasma was repeatedly injected into the original animal, and determinations of antibody were performed by gel diffusion, passive haemagglutination (PH¹⁰), passive cutaneous anaphylaxis (PCA¹¹), and complement fixation¹². In a subsequent trial, materials coated with autologous plasma protein were exposed to autologous peritoneal macrophages¹³ which were then injected back into the donor animal. Determinations of antibody formation were then performed by observing for complement fixation on the surface of the coated materials.

Table 1 Detection of Immunogenicity in Various Materials

Material	Passive haemagglutination	Passive cutaneous anaphylaxis	Complement fixation		
	Autologous antigen	HGG antigen	Autologous antigen	HGG antigen	
Carbon-coated ZrO ₂	3/4 *	0/4	3/4	3/4	0/2
Carboxymethyl cellulose	2/4	0/4	1/4	1/4	2/5
Electrified estane	0/4	0/4	0/5	0/5	0/5
Flexible epoxy	1/4 †	3/4 †	0/4	0/4	1/1
Epoxy with 'Ajicure'	5/5	2/5 †	0/5	1/5	0/5 ‡
Epoxy with 'Ajicure' + 'Pluronic F68'	4/4 †	3/5 †	0/5	0/5	0/5
Epoxy with 3% heparin	3/5 †	4/5	2/5	0/5	0/2
Epoxy with 7% heparin	0/5	4/5	0/4	0/4	1/5 ‡
Heparin bonded to TDMAC	3/4	1/5	0/4	2/5	1/5
'Ioplex'—anionic	2/4	4/4	2/5	2/5	0/4
'Ioplex'—cationic	4/5	0/5	2/5	2/5	0/5
Parylene C	0/4	0/4	0/5	0/5	§
Polyacrylamide	0/4	0/4	0/5	1/5	0/5
Block polyurethane	2/4 †	0/4	0/4	0/4	0/5 ‡
Sialic acid—cholesterol complex	0/4	0/4	0/5	2/5	1/5
Silicone elastomer	0/5	0/5	1/5	0/5	0/5
Heparinized silicone rubber	1/5	0/5	0/5	0/5	0/5

* No. of positives per total number of rabbits tested.

† Weakly positive, titres⁻¹ = 4 to 16.

‡ Results masked by anti-complement effects of coated material without antiserum.

§ Not done.

In an initial series of control experiments with plasma alone, no evidence for antibody formation could be obtained by the above methods. When samples of materials were incorporated into the containers, however, positive reactions were obtained frequently with PH and PCA detection methods with auto-

logous as well as human γ -globulin antigens (Table 1). Precipitin lines were not detectable in gel diffusion with autologous plasma antigen, but infrequent positives were observed with human γ -globulin antigen. Occasional positive results were also observed with complement fixation tests for antigen-antibody reaction at the surfaces of the materials. Because of the qualitative nature of the exposure system, valid comparisons of relative immunogenicities were not possible.

Table 2 Complement Fixation Reactions elicited by Coated Materials and Antisera produced by Injections of Exposed, Autologous Macrophages

Material	No. of positives per total No. of rabbits tested
Epoxy	3/3
Epoxy with 7% heparin	2/9
'Ioplex'—anionic	0/4
'Ioplex'—cationic	—*
Silicone elastomer	—*
Heparinized silicone rubber	0/4

* Coated materials alone showed anti-complement effect.

Of six materials examined by coating with autologous protein and exposing to autologous peritoneal macrophages, only two gave positive tests for antibody formation (Table 2). Anti-complement effects of cationic ioplex and silicone elastomer rendered results with these materials equivocal, and suggested that certain surfaces might deform adsorbed protein to expose complement-reacting groups, or might adsorb anti-complement components selectively.

These results indicated that exposure to large surface areas of foreign material may induce immunogenic changes in autologous rabbit plasma proteins. Low but significant titres were consistent with the type of response to be expected for small amounts of materials with poor immunogenicity¹⁴. Development of antibodies against human γ -globulin may have reflected subtle denaturation of the rabbit γ -globulin plasma component as described by Milgrom and Witebsky¹⁵. The demonstration of responses with whole, exposed plasma as antibody-detecting antigen, moreover, suggested components in addition to γ -globulin may have been rendered immunogenic, but it was unlikely that deeply-buried antigenic determinants¹⁶ were unmasked by procedures employed in these studies.

Whether antigenic stimulation and subsequent pathogenesis may occur as the result of prosthesis implantation in animals or in man has yet to be established. The aetiology of autoimmune haemolytic anaemia associated with open heart surgery alone, or in combination with prosthetic aortic valve implantation, is still unknown¹⁷, and immunogenic interactions of protein with foreign polymer surfaces, either in oxygenators or the implanted prosthesis, have not been excluded¹⁸. One factor predisposing to autoimmune disease, the accumulation of lymphoid cells, is an accompanying feature of some foreign material implants¹⁹. Continuous stimulation of such lymphoid cells by adsorbed, denatured, autologous protein in man would provide an additional predisposing component²⁰.

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Demonstration of Carcinoembryonic Antigen in Normal Human Plasma

CARCINOEMBRYONIC antigen (CEA) was first reported by Gold and Freedman as a tumour-specific antigen found in tissue extract of adenocarcinoma of human colon and not present in normal colonic tissue^{1,2}; also, CEA has been detected in the plasma of patients with other malignant diseases³⁻⁶, and small quantities have also been found in normal colon and lung⁷⁻⁸. We report the results of our studies on the demon-

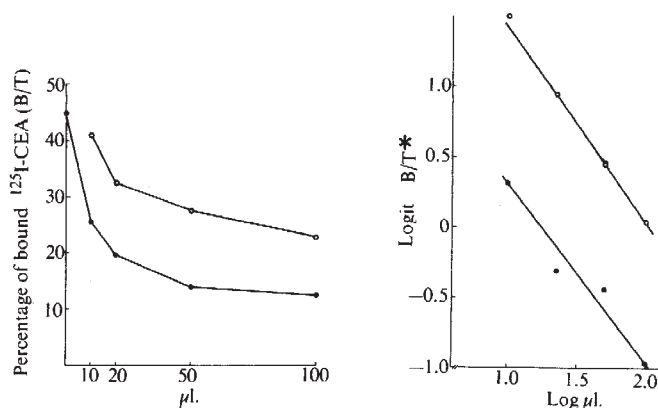


Fig. 1 Standard inhibition curves of reference CEA and lyophilized PCA plasma extract by radioimmunoassay. ●, Standard CEA, 45 ng/1 ml.; ○, lyophilized plasma extract, 30 mg/1 ml.

stration of CEA in plasma of normal healthy individuals by radioimmunoassay and column chromatography.

Plasma from normal healthy persons was pooled to obtain a total of 800 ml. Each sample used in the pool had been previously assayed individually and shown to contain less than 2.5 ng CEA/ml. The pooled plasma was diluted with 2,400 ml. of 0.9% sodium chloride, and the solution extracted with 3,200 ml. of 1.2 M perchloric acid (PCA) solution. The supernatant was dialysed for 72 h against distilled-deionized water and the dialysate lyophilized. A total of 750 mg of lyophilized residue was obtained.

The radioimmunoassay was carried out by incubating standard CEA obtained from colonic carcinoma tissue or lyophilized PCA plasma extract with ^{125}I -CEA and mono-specific, goat anti-CEA antiserum⁹. The antibody-bound ^{125}I -CEA was separated from the free fraction by zirconyl phosphate gel. Fig. 1 shows that the inhibition curves obtained from "true" colonic CEA and lyophilized PCA extract of normal human plasma are similar, and that a parallel plot of the two inhibition curves can be obtained¹⁰. These findings indicate an identity of immunological reaction between PCA extract of normal plasma, and standard solutions of CEA obtained from colon adenocarcinoma. The concentration of CEA in the lyophilized PCA residue equals 1.1 ng/ml. of original plasma.

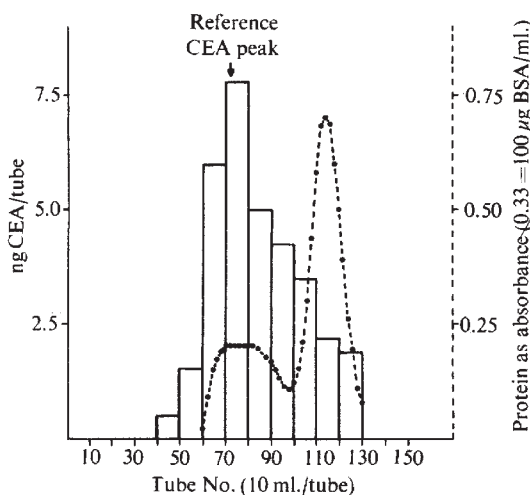


Fig. 2 'Sephadex G-200' column chromatography of lyophilized PCA plasma extract. NaH_2PO_4 , 0.05 M, was used to elute the column.

Further characterization of CEA in PCA extract was carried out by column chromatography: 200 mg of the lyophilized extract was dissolved in 20 ml. of NaH_2PO_4 solution, 0.05 M, and fractionated (10 ml.) in a G-200 chromatographic column (4×90 cm). Every ten fractions were pooled, dialysed, then the CEA activity was assayed by radioimmunoassay. The results are shown in Fig. 2, which shows that fractions 40–130 contain proteins which inhibit the CEA/anti-CEA reaction with a maximal CEA activity in fractions 70–80. The chromatographic pattern is similar to that of standard colonic CEA, which shows maximal inhibitory activity at fraction 72. A total of 358 ng of CEA was recovered from the column, or the equivalent of 1.68 ng/ml. of original plasma, a value consistent with the 1.1 ng/ml. obtained by radioimmunoassay of the crude lyophilized residue.

This may be considered as evidence for the existence of carcinoembryonic antigen in normal adult plasma. The concentrations found in normal adults are, indeed, extremely small, especially when compared with the 80 or 90 ng/ml. which can be found in certain patients with disseminated carcinomas. Nevertheless, with CEA the difference between

normal adult plasma and the plasma of cancer patients is quantitative rather than qualitative, as was formerly believed.

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Persistent Infection of Human Lung Cells with Influenza Virus

INFLUENZA has long been considered to be of relatively short duration in the infected individual¹. The optimal period for isolating the virus from the upper respiratory tract is reported to be during the first 48 h of the disease², and viral antigen is not detectable in these cells beyond 8 days after infection³. These reports, coupled with the general failure to isolate influenza virus from normal individuals between epidemics, suggest that the period of association between influenza virus and its host cell is relatively short, and that the virus is eliminated rapidly. Studies involving the infection of avian lung cells have, however, shown that not all infected cells are killed, and that some cells continue to release virus for prolonged periods⁴. We now have evidence that influenza virus can persistently infect human lung cells, infectious virus being released from the cells for up to 7 weeks after initial infection.

We used the PR8 strain of influenza A virus prepared as described before⁵. Primary monolayer cultures of human lung cells were prepared by constantly agitating finely minced embryo lung tissue in a 0.1% solution of trypsin in phosphate-buffered saline (PBS) at room temperature. The resulting supernatant was discarded after 10 min, replaced by fresh trypsin and thereafter the supernatants were collected at 5 min intervals. Cells were pelleted from the supernatants by centrifugation at 250g for 5 min, resuspended in growth medium (TC 199 with 20% foetal calf serum); the cells obtained after ten to twelve trypsinizations were pooled, dispensed in 3 ml. aliquots into 6 cm diameter 'Falcon' plastic Petri dishes at a concentration of 0.5×10^6 cells/ml., and incubated at 37° C in an atmosphere of 5% CO_2 in air.

Cultures of human lung cells were infected with PR8 virus at multiplicities of 0.25, 2.5 and 12.5 infectious doses (ID_{50}) virus per cell, and virus haemagglutinin release was measured

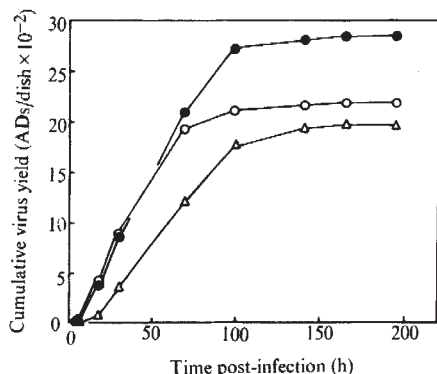


Fig. 1 Cumulative virus yield from primary monolayer culture of human embryo lung cells infected at multiplicities equivalent to 12.5 (○), 2.5 (●) and 0.25 (△) virus particles per cell. Cells were infected as previously described for chick lung cells⁴, and virus release measured by haemagglutination assay⁵, each point being the mean virus yield from four replicate cultures.

at various intervals up to 200 h after infection. Cells infected with 2.5 and 12.5 ID₅₀ per cell released equal amounts of viral haemagglutinin at the same rate up to 27 h post-infection; however, between 72 and 100 h there was a marked decrease in the rate of haemagglutinin release from the cells infected at the higher multiplicity (Fig. 1). In addition, cells infected at the highest multiplicity showed the maximum cytopathic

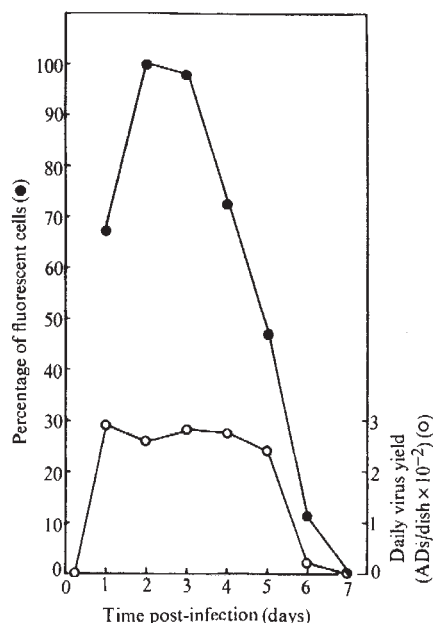


Fig. 2 Virus yield and percentage of human lung cells showing specific fluorescence at various times following infection with PR8 virus at a multiplicity of 2. 1.3 cm diameter disks were cut from 'Falcon' plastic Petri dishes, placed in small bottles and 1 ml. of medium containing 10⁴ human embryo lung cells added to each bottle and the bottles were incubated at 37° C in 5% CO₂ in air. On forming a complete monolayer the cells were infected with PR8 virus at a multiplicity of two virus particles per cell and at various times post-infection four disks were removed from their bottles, washed six times in PBS, fixed by immersion for 1 min in 30%, 50% and 70% methanol respectively, followed by 30 min in 95% methanol. 0.2 ml. of rabbit anti-PR8 virus antiserum was placed on each disk, left for 30 min at room temperature, and then the disks were given three 10-min washes in PBS and stained with fluorescein-conjugated goat anti-rabbit globulin for 30 min at room temperature. Following further washing for 15 min in PBS, the disk cultures were mounted in 95% glycerol in PBS on a glass slide and examined with a Zeiss 'Ultraphot II' fluorescence microscope and the cells showing specific fluorescence counted and expressed as a percentage of the total.

changes. Since the highest rate and level of haemagglutinin release with minimum cytopathic effect was obtained from those cultures infected at a multiplicity of about 2 ID₅₀ per cell, this was used in all other experiments.

To determine cell susceptibility to primary virus infection, the percentage of human lung cells infected initially with PR8 virus at a multiplicity of two per cell was determined using an indirect, fluorescent labelled antibody technique. At 48 h after infection all lung cells exhibited positive fluorescence, indicating that they all contained PR8 virus antigens (Fig. 2). Although the results do not indicate the proportion of cells releasing infectious virus, they do show that there were no virus resistant cells in the population.

Human lung cells were infected at a multiplicity of 2 ID₅₀ per cell, and the surviving cells, which had formed complete monolayers by 6 days after infection, were subcultured at regular intervals for up to 52 days following initial infection. Beyond 5 days after infection, virus release as measured by haemagglutination assay was irregular, and suggested that the method was not sufficiently sensitive to detect small amounts of virus, and thus virus release was measured by titrating for the presence of infectious virus in the culture medium⁶.

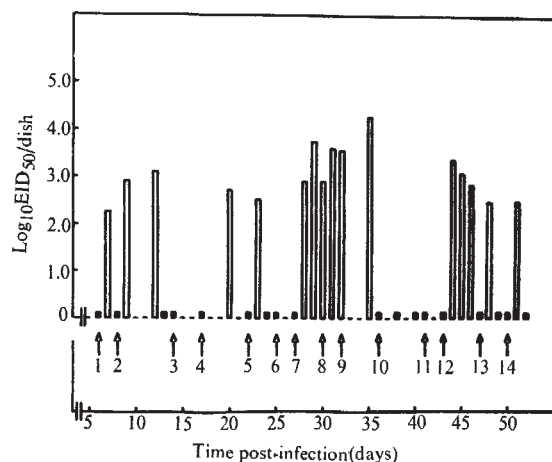


Fig. 3 Infectious virus released from human embryo lung cell cultures at intervals following infection with PR8 virus at a multiplicity of 2 virus particles per cell; numbers 1-14 indicate that cell monolayers were subcultured. Infectivity titrations were carried out as previously described⁴ and titres expressed as egg infectious doses (EID₅₀) per dish. ■, < 10^{2.2} EID₅₀ per dish; —, assay not made.

Infectious virus was released from infected cells at intervals up to 51 days after infection, and was detected in the medium following each subculture (Fig. 3). Failure to detect virus in the medium after four of the subcultures (Nos. 3, 6, 10, 11) could be explained by the fact that the medium was not changed for 48-72 h after each of the above four subcultures, compared with every 24 h for the other medium changes. The relatively small amounts of infectious virus present in the medium are considered to have been thermally inactivated by remaining at 37° C for 48-72 h before testing for infectivity. This we have been able to confirm by demonstrating that the infectivity of PR8 virus in growth medium at 37° C fell by a factor of 10⁴ ID₅₀ per dish over a 50 h period.

The PR8 strain of influenza virus has been shown to establish a persistent infection in human lung cells with the release of small amounts of infectious virus over a 7-week period following initial infection. After the first 5 days, the appearance of infectious virus in the cultures seemed to follow subcultivation of the cells (Fig. 3). It was suggested that this may have been due to the action of the trypsin, used for subculturing, inactivating the interferon being released by the cells. This explanation now seems unlikely, as we have been able to demonstrate that

although a viral inhibitor was present in the cultures, it could be found only up to a maximum of 6 days after infection, and thus destruction of such an inhibitor by trypsin could not account for the observed release of virus from infected cells between 6 and 51 days after infection. It is possible, however, that the replication of influenza virus in the persistently-infected human lung cells is related directly or indirectly to cell DNA turnover, since virus release seemed to follow subcultivation of the cells and it has been shown that cell DNA synthesis occurs at a higher rate in recent subcultures than in resting cultures (for example, complete cell monolayers⁷).

As influenza virus can establish a persistent infection in normal human respiratory tissue grown *in vitro*, one could speculate that naturally-occurring influenza virus infections may not be so rapidly self-limiting as the relatively brief duration of the uncomplicated clinical illness would indicate, although further studies would have to be undertaken to test this hypothesis.

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Persistence of Methadone-³H and Metabolite in Rat Brain after a Single Injection and its Implications on Pharmacological Tolerance

BECAUSE of its properties of effective suppression of opiate withdrawal symptoms for long periods, oral absorption, longer duration of action and slow excretion, methadone has been widely used for social rehabilitation and adjustment of chronic heroin users^{1,2}. In spite of much work³⁻¹⁰, the basic mechanism of pharmacological tolerance to methadone remains obscure. The ability of metabolic inhibitors to reduce the analgesic response significantly in experimental animals, and the lack of correlation between observable morphine-like effects and drug concentrations in tissue, has led to the suggestion that a metabolite of methadone may be responsible for its effects¹¹⁻¹³.

The recently isolated substituted pyrrolidine and pyrroline metabolites of methadone¹⁴⁻¹⁷, however, have been found to be pharmacologically inactive. This study demonstrates for the first time the persistence in the rat brain of methadone and a metabolite initially in the free form and later as a protein-conjugate after a single subcutaneous injection for periods up to 3 weeks (longer periods were not investigated). The implications of these findings on pharmacological tolerance are discussed here.

Male Wistar rats (120-150 g) were injected subcutaneously with a 10 mg/kg dose of laevomethadone-1-³H (New England Nuclear, Boston, radiochemical purity 99.2%) (specific activity 5 μ Ci/mg) and decapitated at different periods of time; the cerebral cortical hemispheres were removed, wiped of adhering blood by soft tissue paper, rinsed in ice-cold saline, rewiped and weighed. Free methadone-1-³H was determined by homogenization of brain in 0.5 M HCl (20% homogenate), adjusting the pH of a 2 ml. aliquot of homogenate containing 1 ml. nonradioactive methadone carrier (500 μ g/ml.) with dilute NaOH to pH 9.5; this was buffered with 2 ml. 40% K₂HPO₄ solution and extracted with 15 ml. ethylenedichloride containing 20% v/v of isopropanol by shaking for 30 min and the organic phase was centrifuged and washed with 4 ml. 4% K₂HPO₄. The residue obtained by evaporating 10 ml. aliquots of organic phase in counting vials was dissolved in 0.5 ml. isopropanol and radioactivity counted with 10 ml. toluene phosphor solution. *In vitro* recoveries of methadone-³H from rat brain homogenates by this method were quantitative. Total radioactivity was determined by the method previously described¹⁸ and counts corrected for quenching using toluene-³H as internal standard. The mean values of uptake of methadone-³H by rat cerebral cortical hemispheres at different times after a single subcutaneous injection and a single oral dose of 10 mg/kg are given in Table 1.

The qualitative identification of methadone-1-³H and metabolite was done on groups of four brains removed 1, 6 and 12 h after a single subcutaneous injection of 10 mg/kg. The brains were homogenized in 0.5 M HCl and processed by two different methods. In one, the homogenate was adjusted to pH 9.5, repeatedly extracted with chloroform-isopropanol (3:1, v/v), and the residue from pooled organic extracts, aqueous phase and ethanolic extracts of brain debris taken up in a small volume of methanol for thin layer chromatography by Gelman instant thin layer chromatography media, silica gel (ITLC); in the second, the brain homogenate in 0.5 M HCl was centrifuged and the supernatant neutralized to pH 7, chromatographed on 'Amberlite' XAD-2 and the residue from methanolic-ammonia (300:5, v/v) eluate subjected to TLC in different solvent systems. The radioscan of thin layer chromatograms (Fig. 1) show two peaks, one with higher *R_f* due to methadone-³H (a), and the second near the origin due to its metabolite (b). Further confirmation of the presence of metabolite was obtained on buffered paper and TLC¹⁹ using selective solvent systems, and it was thus possible to rule out the formation of methadone N-oxide, N-methyl methadone, methadol, acetyl methadol, and substituted pyrrolidine and pyrroline metabolites. The metabolite possessed phenolic OH and primary amine groups and has also

Table 1 Uptake of Methadone-1-³H by Rat Cerebral Cortical Hemispheres at Different Times after a Single 10 mg/kg Dose by Subcutaneous Injection or Oral Administration*

	30 min	1 h	2 h	4 h	6 h	12 h	24 h	48 h	96 h	5 days	1 week	3 weeks
Injection: (a) Extractable radioactivity (free methadone)	3,869.0	4,502.2	2,717.2	1,313.7	854.6	60.1	25.2	27.1	26.7	15.4	20.2	21.3
(b) Total radioactivity	—	4,804	—	—	1,068	—	288.3	—	—	—	110.4	—
Oral, extractable radioactivity (free methadone)	138	179	—	153	80.7†	30	22	9.3	—	—	20.6	15.9

* Data represent the mean value (ng/g wet brain weight) of four animals up to 24 h and two animals for later time periods and total radioactivity determinations.

† The figure represents the uptake 8 h after oral administration instead of 6 h.

been observed as a urinary excretion product in the rat (unpublished results). Oxidative N-demethylation to a des-methyl derivative, an important metabolic pathway for methadone^{9,20}, leads primarily to substituted pyrrolidine and pyrroline metabolic products¹⁴⁻¹⁷. Methadol with a secondary alcohol group in place of ketone has been reported to be more readily N-dealkylated than acetyl methadol¹². The presence of a secondary alcohol group prevents cyclization of the N-demethylated product and the methyl group in α -position to the primary amine group hinders oxidative deamination of the amino group.

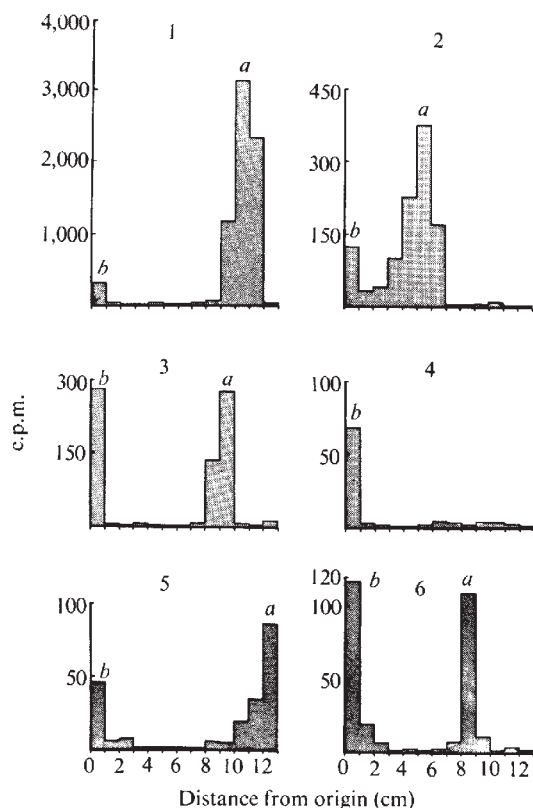


Fig. 1 Radioscans of thin layer chromatograms of chloroform-isopropanol extract of rat brain 1 h after a 10 mg/kg subcutaneous injection of methadone-³H: (1) silica gel, in solvent system S₁; benzene-ethyl acetate-methanol-concentrated ammonia (80:20:1.2:0.1, v/v); (2) alumina, in benzene-n-butyl ether (19:1, v/v); (3) brains 6 h after injection processed on 'Amberlite' XAD-2 resin and thin layer chromatograms (silica gel), in solvent system S₁; (4) rechromatography of eluted polar metabolite from (3) in S₁; (5) brains 12 h after injection processed as under (3) in solvent system, ethyl acetate-methanol-conc. ammonia (17:2:1, v/v); (6) in solvent system S₁.

The persistent association of radioactivity with brain debris, even after extraction with 0.5 M HCl, suggested a firm binding of methadone-³H or its metabolite with some specific intracellular constituent. The reversible binding of methadone with brain proteins can be disrupted by treatment with dilute acids. It would appear therefore that electrostatic and Van der Waals-London forces do not contribute significantly to the firm binding of metabolite with brain tissue. Brain proteolipids²¹ have been recognized as important structural components of membranes and are implicated in neurohumoral function^{22,23} and drug-receptor interactions²⁴. These proteolipids bind biogenic amines reversibly and irreversibly through a covalent amide linkage involving the primary amine group²⁵⁻²⁷. The persistence of methadone in the brain presumably involves association of the keto group of methadone with terminal amino group of protein. The firm binding of the metabolite with brain protein might occur through a covalent amide linkage involving the amino group of the

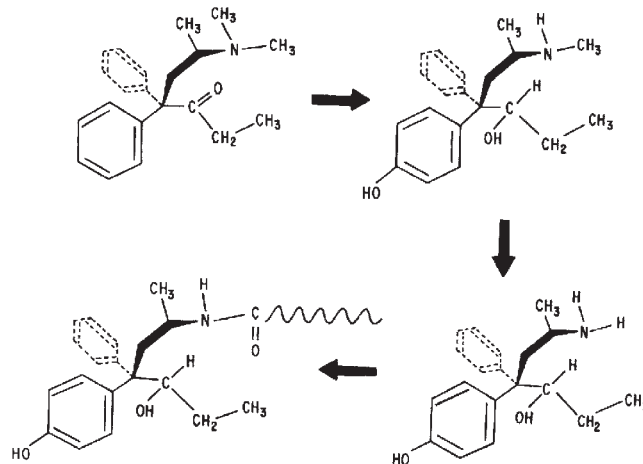


Fig. 2 Outline of scheme showing the N-demethylation of methadone metabolite and the probable site of covalent amide linking with intracellular brain protein.

N-dealkylated methadone and carboxylic group of some specific brain protein (Fig. 2). Partial structural similarity of the metabolite to noradrenaline and prolonged occupation of the receptor site may well be responsible for the development of pharmacological tolerance and comparatively mild withdrawal symptoms observed with methadone.

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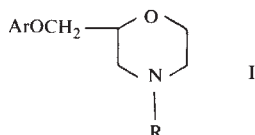
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2-(2-Ethoxyphenoxyethyl)tetrahydro-1,4-oxazine Hydrochloride, a Potential Psychotropic Agent

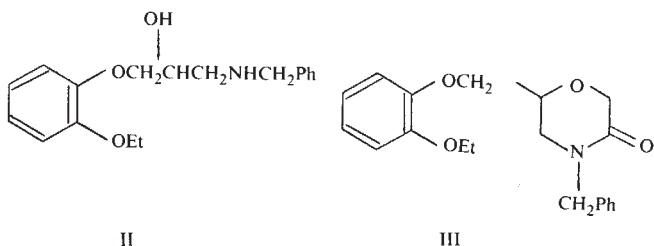
We have been investigating the pharmacological properties of a series of aryloxyethyltetrahydro-1,4-oxazines of the general formula (I):



where Ar is an aromatic group (optionally substituted), and R is hydrogen or an alkyl group. The series arose from attempts to exploit the observed activity of the aryloxypropanolamine series of β -adrenergic blocking agents on the central nervous system of laboratory animals^{1,2}. To obtain more lipophilic compounds, a two-carbon bridge was inserted between the amine nitrogen and hydroxyl group, leading to compounds of the formula (I).

Potent actions on the central nervous system (CNS) of animals were found in many of these compounds. Those members of the series in which R = H had, in general, the most marked CNS effects, and were devoid of β -adrenergic blocking properties.

One of the more interesting compounds of the series is ICI 58,834 (I, R = H, Ar = 2-ethoxyphenyl) which can be prepared as follows³. *o*-Ethoxyphenol is reacted with epichlorohydrin in basic conditions, and the resulting aryloxypropylene oxide is heated with benzylamine to give the propanolamine (II). The N-chloroacetyl derivative of (II) is then cyclized in basic conditions to give the cyclic amide (III). Reduction of (III) with lithium aluminium hydride, followed by hydrogenation to remove the benzyl group, yields ICI 58,834 which is conveniently isolated as the hydrochloride, melting point 185°–186° C. Its structure has been established by infrared, ultraviolet, nuclear magnetic resonance and mass spectrometry.



In mice, ICI 58,834 (0.3–1.0 mg/kg orally) was shown to reverse and to prevent reserpine or tetrabenazine-induced hypothermia and ptosis, and in these tests it was equipotent with the tricyclic antidepressant drug, desmethylinipramine. Given intravenously (0.3–2.0 mg/kg) to anaesthetized cats it potentiated the contractile responses of the nictitating membrane to preganglionic electrical stimulation of the ascending sympathetic trunk (20–25% increase) and also those elicited by intravenous injections of noradrenaline or 5-hydroxy-

tryptamine (100–200% increase). *In vitro*, in small concentrations ($1\text{--}5 \times 10^{-7}$ g/ml.), it potentiated the action of noradrenaline on the isolated rat vas deferens, as does desmethylinipramine, but at greater concentrations ICI 58,834 alone induced dose-related contractions of this tissue. In this respect its action is reminiscent of that of amphetamine. Observations of the effect of the compound on the electrocortical activity of conscious rats showed that at 10–25 mg/kg intraperitoneally, it too caused desynchronization of the electroencephalogram, as did amphetamine at one-tenth of this dose. This similarity with amphetamine was confirmed by simultaneous frequency analysis (J. G. B. and G. B. Horsfall, work in preparation) which revealed reduced activity at 7.5 and 15 Hz.

Taken alone, the foregoing observations could be interpreted as indicating that ICI 58,834 has amphetamine-like stimulant properties. Amphetamine and similar psychomotor stimulants have, however, other effects in laboratory animals. For example, they increase locomotor activity⁴, induce hyperthermia in mice maintained at elevated ambient temperatures⁵ and cause characteristic sympathomimetic and behavioural signs in non-rodent species^{6,7}. ICI 58,834 had none of these effects. Indeed, with larger doses than those yet mentioned, it showed activity in a number of neuropharmacological tests which indicates that it is a CNS depressant of higher potency and lower toxicity than many known CNS drugs. Thus, in mice, in oral doses of 10–30 mg/kg, it reduced locomotor activity, potentiated hexobarbitone induced hypnosis and protected from convulsions induced electrically or with pentyl-enetetrazole. In similar doses it also protected rats from electrically induced convulsions, and, at 10 mg/kg intraperitoneally, had a calming effect on rats made aggressive by septal lesions⁸. A high degree of selectivity in the above tests is indicated by our findings, in mice, of low neurotoxicity (rotating rod ED₅₀ = 250 mg/kg, orally) and low acute lethality (LD₅₀ = 1,000 mg/kg, orally).

Using assays based on published methods (refs. 9 and 10, and A. R. S., work in preparation) we have shown that, *in vitro*, ICI 58,834 is not an inhibitor of monoamine oxidase (3% inhibition at 100 μ g/ml.; compare 40% inhibition by mebanazine at 1 μ g/ml.) or of catechol-O-methyltransferase (4% inhibition at 100 μ g/ml.). Nor did it significantly inhibit the uptake of 5-hydroxytryptamine by human blood platelets (4% inhibition at 10 μ g/ml.; compare 54% inhibition by imipramine at 0.1 μ g/ml.). ICI 58,834 is thus a compound with a novel profile of neuropharmacological activity, possessing features in common with both amphetamine and the tricyclic antidepressants and also with several classes of CNS depressants. It therefore seems that ICI 58,834 is worthy of study in a variety of psychiatric disorders in man.

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Aspirin Prevents the Disruption of the Blood-Aqueous Barrier in the Rabbit Eye

THE acutely traumatized mammalian eye shows an irritative response, characterized by hyperaemia of the conjunctiva and iris, miosis, disruption of the blood-aqueous barrier, and a transient increase in intraocular pressure followed by relative hypotony. One sign of the disruption of the barrier is a positive aqueous flare, with increased concentrations of blood proteins in the aqueous humour. Stimuli that elicit all or part of this response in the rabbit eye include nitrogen mustard instillation in the conjunctival sac¹, subcutaneous injection of melanocyte stimulating hormone (MSH)², stroking the iris^{3,4} or cornea⁵, infrared irradiation of the iris⁶, mechanical stimulation of the trigeminal nerve⁷, and anterior chamber paracentesis⁸.

Prostaglandins may mediate this response^{9,10}. We wish to present evidence that prostaglandins are involved in the disruption of the blood-aqueous barrier in the rabbit eye. Our experiments indicate that aspirin, an inhibitor of prostaglandin synthesis¹¹⁻¹³, reduces the intensity of the irritative response of the rabbit eye to various stimuli.

Male albino rabbits (2-3 kg) were lightly anaesthetized with intravenous sodium pentobarbital. The corneal reflex was present except during paracentesis when the level of anaesthesia was deepened. Experimental animals were given 600 mg aspirin per rectum. Within 1 h this dose produced a concentration of 46 ± 5 mg% (mean $\pm$ s.e.m.) (seven observations) in the serum, and 13 ± 2 mg% (nine observations) in the aqueous humour, determined colorimetrically¹⁴. Control animals were not given aspirin. After 1 h, both eyes of all animals underwent paracentesis. Using a 30 gauge needle, aqueous humour was slowly aspirated from the anterior chamber, evacuating it to the point of collapse and avoiding direct trauma to the iris or lens. The aqueous humour was kept for protein determination. One and a half hours later (2.5 h after aspirin), the anterior chamber had reformed and paracentesis was repeated. This "secondary" aqueous humour was also kept for protein determination. The gross appearance of the control and experimental eyes at the time of the second paracentesis was much different. The eyes of the aspirin-treated group showed slight hyperaemia of the conjunctiva and iris and some miosis. The control group showed marked hyperaemia of the conjunctiva and iris and the same degree of miosis. The aqueous humour of this group appeared orange and clotted. The protein concentration in all aqueous humour specimens was determined by the method of Lowry *et al.*¹⁵ with bovine serum albumin as standard.

The aqueous humour from the first paracentesis had a protein concentration of 60 ± 10 mg% (twenty-eight observations), and was the same in both groups. This agreed well with other published data¹⁶. In the non-aspirin treated group, the protein in the aqueous humour rose in 1.5 h to $2,340 \pm 130$ mg% (fourteen observations) in response to the first paracentesis. The aspirin-treated group rose to 860 ± 50 mg% (fourteen observations). This represented a two-thirds inhibition of the aqueous protein response by aspirin (Fig. 1). Similar results were obtained if each animal was used as its own control; the double paracentesis was performed on one eye, aspirin then administered, and double paracentesis performed on the second eye.

The same experiments performed with male Dutch pigmented rabbits gave comparable results. The aqueous humour from the first paracentesis had a protein concentration of 74 ± 9 mg% (fourteen observations). In response to the first paracentesis, the protein in the aqueous humour of the eyes of control animals increased in 1.5 h to $4,180 \pm 200$ mg% (eight observations). The aqueous humour of the eyes of aspirin-treated animals rose to $2,540 \pm 170$ mg% (six observations). Thus, although there was a greater disruption of the blood-aqueous barrier in the pigmented rabbits than in the albino rabbits, aspirin still inhibited the response (Fig. 2). Slight miosis occurred in both groups.

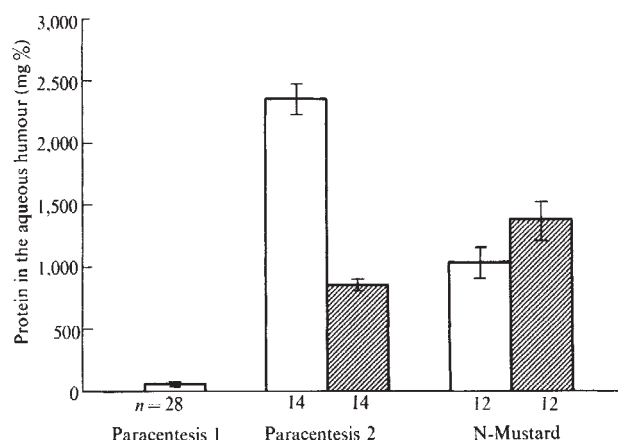


Fig. 1 Protein concentration in the aqueous humour of the albino rabbit eye in response to various stimuli. Paracentesis 1: the normal, undisturbed state. Paracentesis 2: the response to paracentesis 1, 1.5 h later. N-mustard: the response to nitrogen mustard applied to the conjunctiva, 1.5 h later. Hatched columns represent animals pretreated with aspirin; white columns represent the control animals that received no medication. All values are the mean $\pm$ s.e.m., and *n* is the number of eyes in which the observation was made.

Two drops of 1% nitrogen mustard [methyl-bis(β -chloroethyl)-amine HCl] were instilled in the conjunctival sac of two groups of rabbits to produce the irritative response¹. One group was pretreated with 600 mg aspirin per rectum 1 h before instillation. The control group received no medication. Intense miosis occurred with marked conjunctival hyperaemia and chemosis, and some hyperaemia of the iris. Paracentesis performed 1.5 h after the nitrogen mustard demonstrated a rise in aqueous humour protein to $1,033 \pm 130$ mg% (twelve observations). Aspirin did not inhibit this protein rise (Fig. 1). This paracentesis, however, elicited a further protein rise ($2,070 \pm 165$ mg% (sixteen observations)), which was partially inhibited by aspirin. A two- to three-fold increase in intraocular pressure was observed 30 min after administration of nitrogen mustard in both groups.

MSH produces an aqueous flare response in pigmented rabbits². Dutch pigmented animals were given 100-200 mg of racemized beta-MSH subcutaneously. Most of the animals developed aqueous flare and increased aqueous protein. Miosis and conjunctival hyperaemia were not observed. Aspirin failed to inhibit the response; in fact, the highest protein concentration was in an aspirin-treated animal.

Direct trauma to the iris elicits aqueous flare; infrared irradiation⁶ or mechanical stroking⁴ of the iris causes increased protein in the aqueous humour. We have used argon laser radiation as a reproducible and quantifiable physical stimulus. Twenty-five to thirty laser pulses, 0.2 s duration, at 0.25 W, were delivered to the irises of two groups of Dutch pigmented rabbits. One group was treated with aspirin 1 h earlier. All animals showed moderate miosis immediately after treatment which lessened over the next hour. Burns were grossly visible on the iris. One and a quarter hours after laser treatment,

paracentesis was performed and the aqueous protein determined. The protein concentration of the aqueous humour of the control animals rose to $1,353 \pm 280$ mg % (eight observations). The aqueous humour of the aspirin-treated animals rose to 365 ± 80 mg % (ten observations). Aspirin thus significantly inhibited the aqueous protein response to laser irradiation of the iris (Fig. 2).

Specific biochemical mechanisms for the development of the irritative response have only recently been investigated. Ambache showed that an ether-soluble extract from the iris had smooth-muscle-contracting and vasodilating properties¹⁷. The active extract was called irin and later was identified as a mixture of prostaglandins, PGE_2 and $\text{PGF}_{2\alpha}$ ¹⁸. Prostaglandins, administered to the eye, reproduce the components of the irritative response. The miosis produced by trigeminal stimulation or by direct irritation of the iris is mimicked by administration of some of the PGEs ^{21,22}. This is compatible with the resistance of this miosis to autonomic blockade²³. Prostaglandins can raise the intraocular pressure when injected intracamerally and can increase aqueous protein¹⁰. It seems reasonable to hypothesize that the stimuli for the irritative response provoke prostaglandin synthesis.

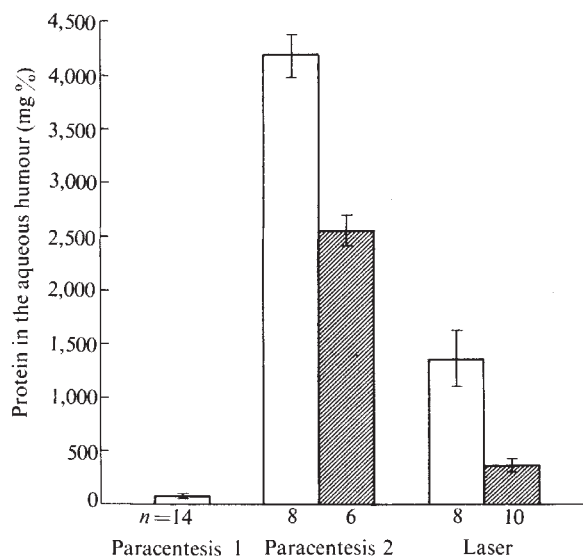


Fig. 2 Protein concentration in the aqueous humour of the Dutch pigmented rabbit eye in response to various stimuli. Paracentesis 1: the normal, undisturbed state. Paracentesis 2: the response to paracentesis 1, 1.5 h later. Laser: the response to laser irradiation of the iris, 1.25 h later. Hatched columns represent animals pretreated with aspirin; white columns represent the control animals that received no medication. All values are the mean $\pm$ s.e.m., and n is the number of eyes in which the observation was made.

Aspirin has been shown to inhibit synthesis of prostaglandins E_2 and $\text{F}_{2\alpha}$ ¹¹⁻¹³. In our experiments, aspirin significantly diminished the *in vivo* response to ocular trauma. In albino and pigmented rabbits, aspirin markedly inhibited the rise in aqueous protein after paracentesis. In pigmented rabbits, aspirin also largely prevented a rise in aqueous protein in response to laser irradiation of the iris. Thus the irritative response appears at least partially mediated by prostaglandins whose synthesis is inhibited by aspirin.

In some instances other mediators or aspirin insensitive prostaglandins may have been active. Aspirin did not entirely inhibit the protein rise in response to paracentesis or irradiation of the iris, and was ineffective in preventing the small protein rise in response to MSH. Nor did it prevent the protein rise in animals treated with nitrogen mustard. The miosis which occurred in most of the experiments was also not prevented by aspirin. The possibility that the dose of aspirin used was not sufficient has not been ruled out. The irritative response

has seemed historically to be a unified response elicited by a variety of stimuli. It is now apparent that its components are separately provoked by different chemical mediators. These responses require the presence of an intact innervation^{4,6} but detailed study of the interaction between nervous stimuli and synthesis and release of prostaglandins has not been done. Anatomical and pharmacological studies are in progress to determine the various mediators and receptors for these different components.

We suggest the following mechanism for the development of one of the components of the irritative response, that is, increased protein in the aqueous humour. Trauma to the eye results in prostaglandin synthesis and release into the aqueous humour. Uptake of prostaglandins by the ciliary body has been demonstrated²⁴, and may be related to the formation of Graafian vesicles²⁵ and the breakdown of the blood-aqueous barrier.

Certain potentially useful applications are implied by our findings. The blood-aqueous barrier of the rabbit is particularly sensitive to trauma. In many laboratory investigations an intact barrier is required, for example, in studies of aqueous humour dynamics. Pretreatment of animals with aspirin will prove helpful in stabilizing the blood-aqueous barrier.

The aqueous protein response is not peculiar to the rabbit eye, but has its counterpart in man. Aqueous flare and miosis occur after trauma, for example, corneal abrasion. In addition, intraocular surgery and uveitis cause disruption of the blood-aqueous barrier. Salicylates have been used in certain forms of uveitis²⁶. It is possible that prophylactic or therapeutic treatment with aspirin may be helpful in a number of human clinical conditions.

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Physiological Colour Change in the Hercules Beetle

THE Hercules beetle, *Dynastes hercules* L., can change the colour of its elytra—horny fore-wings—from black to greenish yellow and back again to black all within a few minutes. It does this in a way previously unknown among insects. Apart from the reversible migrations of pigment granules in the iris cells, physiological or rapidly reversible colour changes are very rare in insects¹⁻⁴. Among beetles, *Coptocyclia*⁵, *Aspidomorpha*, and many other Cassidinae can change the colour of their elytra by varying the amount of water in the cuticle and thereby the thickness of the thin films responsible for the interference colours.

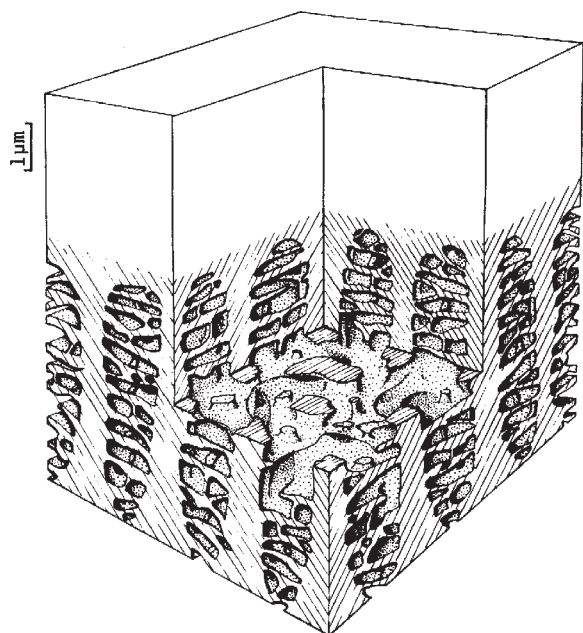


Fig. 1 The yellow spongy layer of the elytra beneath the transparent epicuticle.

The outermost layer of the cuticle of the Hercules beetle is transparent and about 3 μm thick. Below is a yellowish spongy layer generally about 5 μm thick. Below the yellowish spongy layer the cuticle is black by reflected light and reddish by transmitted light. Transmission electron micrographs show that the spongy layer consists of columns or pillars normal to the plane of the surface and usually about 0.5 to 1 μm thick. The pillars are connected to each other by irregular branches normal to their major axes (Fig. 1). When the elytra are yellowish, the spaces between the pillars are filled with air; when the elytra are black, the spaces between the pillars are filled with liquid. Scanning electron micrographs of 10 μm thick sections show that the spongy layer is much more irregular than would appear from transmission micrographs. The interstices or spaces between the branches of the pillars usually vary from 0.01 to 0.5 μm wide. Columns that are oval or circular in section and up to 1.6 mm in diameter extend vertically through the elytra to the outermost layer. When the elytra are yellowish because the interstices of the spongy layer are filled with air, the areas occupied by the columns appear as black spots.

Air can be squeezed out from the spaces in the spongy layer by exerting a little pressure with a rounded point so that the outermost transparent layer is not broken. The black layer below then shows through the now optically homogeneous spongy layer. Black lines made in this way on old museum specimens (Fig. 2) appear to be more or less permanent. The yellow colour, however, may be restored by adding water to the surface over the black areas and allowing it to evaporate.

The water is absorbed by the spongy layer and restores its interstices, but the colour remains black until the water evaporates and the coloured layer again becomes optically heterogeneous. If a drop of liquid nitrogen is placed on a black elytron of either a live or a dead beetle, a yellow spot immediately appears which vanishes as soon as the nitrogen evaporates and the spongy layer once more becomes optically homogeneous.

If a live beetle that has yellowish elytra is placed in a saturated environment, the elytra become black. If the relative humidity is suddenly reduced to 80% or less, yellow patches begin to appear on the elytra, usually within 30 s–2 min. The rate of yellowing depends on both the previous history of the individual and the temperature. When an elytron was removed from a living beetle, it changed colour in just the same way as the elytron left attached when both were subjected to the same changes in relative humidity.

Colour changes were not affected when male beetles were kept in the light or in total darkness, or by blackening their eyes, or by prodding them or exposing them to sounds of different intensities and frequencies.

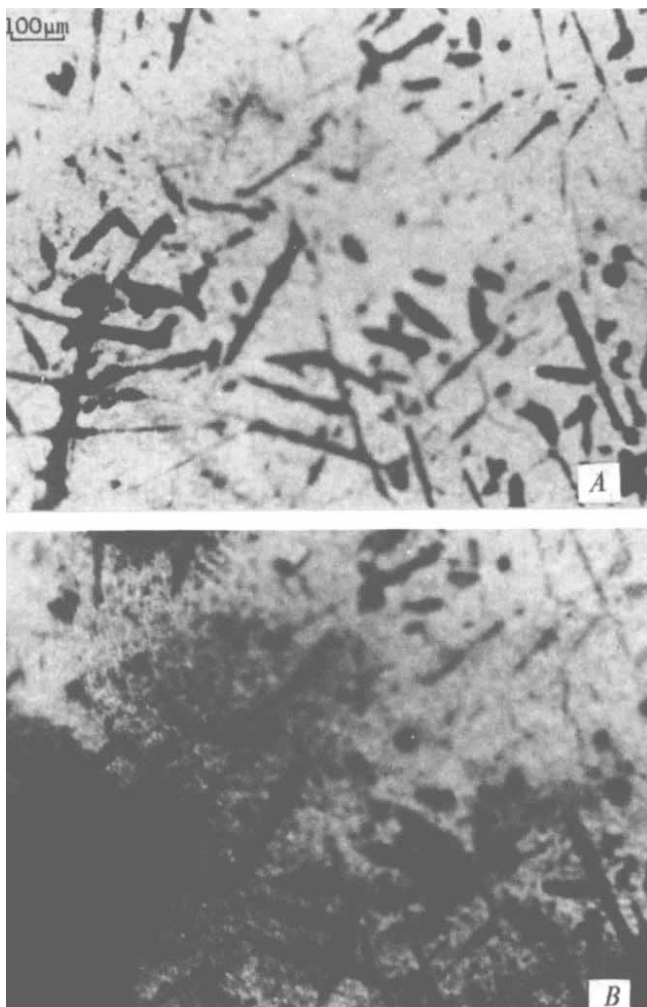


Fig. 2 The gradual flooding of the yellow spongy layer when a piece of an elytron is immersed in gum chloral. A, Shortly after immersion and (B) about 30 min later when many more of the air spaces in the spongy layer are filled with the liquid.

Live beetles kept at a constant humidity invariably became black in time. In one series of experiments, pairs of glass tubes were attached by their open ends, with chewing gum, to the elytra of beetles that were black in saturated air. One tube was filled with silica gel and the other with moist filter paper. The circle under the tube with the silica gel yellowed

immediately but then blackened over a period of many hours. The silica gel remained blue, which is difficult to explain. Perhaps after absorbing a small amount of water, enough lipids were transferred to the area to render it relatively impermeable to water: the hydrocarbons that can be washed with hot chloroform from the surface of the elytra suggest a lipid layer several hundred molecules thick. When the beetles were transferred to a relative humidity of 80%, the elytra became yellowish. When the tube with moist filter paper was removed, the area beneath was always black but then yellowed at about the same rate as the exposed parts of the elytra had done. When the tube with silica gel was removed, the circle beneath it stayed black, perhaps because that area was then subjected to an increase in the ambient relative humidity.

From both the experiments with dead elytra and living beetles, it appears that the level of hydration of the spongy layer, and therefore the colour, is determined by (1) the level of hydration of the spongy layer under direct control, presumably by the epidermal cells of the elytra, and (2) the amount of water that condenses on the surface of the epicuticle and is then absorbed by the spongy layer below.

Experiments with museum specimens suggest that *D. hyllus* Chev., *D. granti* Horn, and *D. tityrus* L. change colour in the same way. In the latter two species the structure of the cuticle of the pronotum is like that of the elytra. Neither the American *D. neptunus* Quenzel nor any of the African or Oriental species of *Dynastes* seem to be able to change colour.

The selective advantage of the colour change may have to do with the fact that whereas a large entirely black beetle is not easily visible at night, it would be more conspicuous than a beetle with yellowish elytra in most situations in a tropical forest during the day. Thus the beetle would be entirely black during the night when the humidity was high, but its elytra would become yellowish as the humidity fell during the day.

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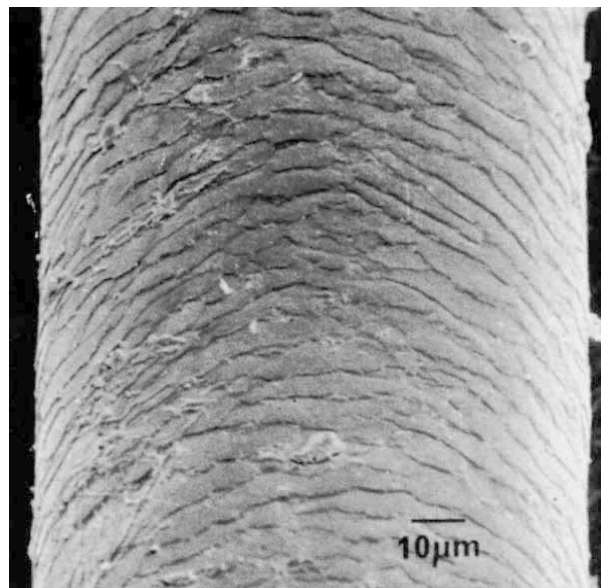


Fig. 1 A typical Jane Austen hair.

operated in the secondary electron emissive mode and at an accelerating potential of 10 kV.

The hairs varied in length up to 40 cm, were from 50 to 80 μm in diameter, slightly elliptical and their surfaces covered with a pattern of overlapping scales as is typical of contemporary Caucasian head hair¹. A most unusual feature was that for at least three-quarters of the length of each hair the scale margins were of smooth contour and the scale surfaces relatively flat (Fig. 1). In recent years we have examined many thousands of hairs from women who apply normal grooming, and the scale margins within the first 2 to 5 cm of the scalp surface are usually of smooth contour, but beyond this the scale margins break away to give highly irregular edges. In addition to this, the scale surfaces, although smooth in the first 2 to 5 cm from the scalp, are punctuated by occasional low ridges and depressions. These changes are normally brought about by the action of brushing, combing and mechanical handling. It must be concluded, therefore, that within the last three years of her life Jane Austen did little to tend her

Scanning Electron Microscope Study of Jane Austen's Hair

JANE AUSTEN (1775–1817) bequeathed a lock of her hair to her niece Fanny Knight. In 1949 this lock, mounted between two glass disks in a gilt frame, came into the possession of the Jane Austen Society and since then has been exhibited in the museum at Chawton in Hampshire. Recently we were approached by the society to examine the hair, for it was thought that some deterioration had occurred. Certainly some bleaching by light had taken place because the side of the lock which was exhibited uppermost was a light straw colour, whereas the underside was mid-brown. As it was desired to preserve the majority of the hair lock intact, our studies have been restricted to the examination of a few of the fibres with the aid of the scanning electron microscope.

Hairs for examination were stuck to double-sided 'Sellotape' on a standard scanning electron microscope mount and vacuum coated with a 10 nm-thick layer of carbon followed by a 30 nm-thick layer of metallic silver. These were examined in a Cambridge 'Stereoscan Mk II' scanning electron microscope



Fig. 2 An engraved portrait of Jane Austen which appeared in Edward Austen-Leigh's memoir².

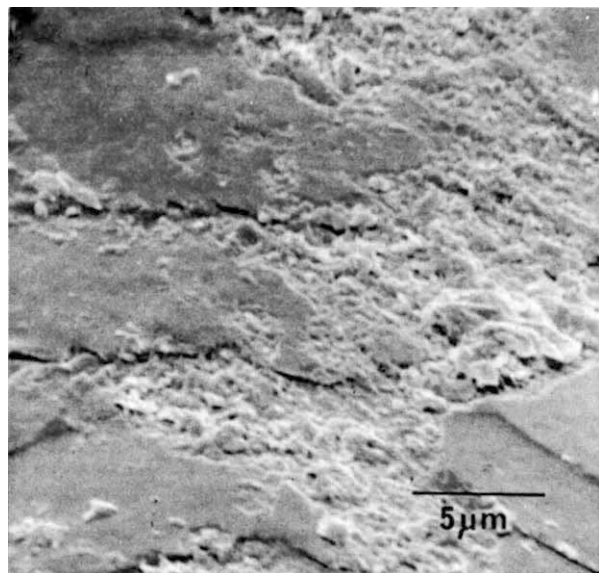


Fig. 3 Jane Austen hair showing erosion of some of the scale surfaces.

hair and that brushing, combing and handling were minimal. It is interesting in this context that her niece Caroline wrote of her: "Her hair, darkish brown, curled naturally—it was in short curls around her face. She always wore a cap—such was the custom of ladies who were not quite young—at least of a morning but I never saw her without one"² (Fig. 2). Perhaps the wearing of this cap offered some degree of protection of the hair from physical damage and might be consistent with an individual who placed little emphasis on the outward appearance of her hair.

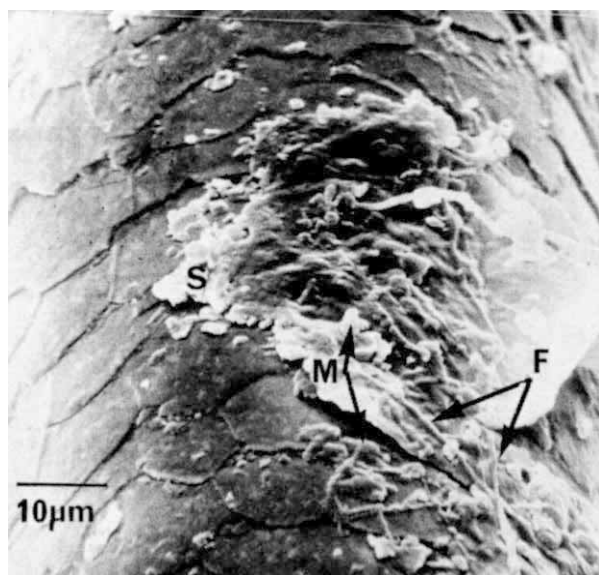


Fig. 4 Jane Austen hair; S, adhering skin flake; F, filaments; M, microorganisms resembling those of the genus *Pityrosporum*.

In some places the hair surfaces have been quite specifically eroded in the form of shallow irregular depressions and occasional craters (Fig. 3). Desquamated skin flakes were also observed interspersed with long filaments of about 0.4 μm diameter, and occasional ellipsoidal bodies about 2 μm long and 0.6 μm diameter were encountered, resembling cells of the naturally occurring scalp yeasts of the genus *Pityrosporum* (Fig. 4)¹. In one case a filament of 0.4 μm diameter and 15 μm long was observed which was connected at one end to the bud

scar of a cell of the *Pityrosporum* genus. This latter filamentous entity is undoubtedly an example of *Malassezia furfur*, a filamentous microorganism which, although not normally encountered on human hair, is known to invade the cornified cells of the skin in a patchy scaling disorder known as *tinea versicolor* (or *pityriasis versicolor*)⁴. Certainly broad filaments similar to this have been observed by us in skin from patients with *pityriasis versicolor* (unpublished results of J. A. S. and R. P. R. Dawber). Although it has been suggested that *Malassezia furfur* is an evasive mycelial form of yeasts of the *Pityrosporum* genus (and particularly *Pityrosporum orbiculare*)^{5,6} we believe that this is the first time direct association between these two microorganisms has been established.

It seems more than probable that the various filamentous fungi have been responsible for the slight surface erosion of the Jane Austen hair. Since no such surface degeneration has been encountered by us in the examination of many thousands of contemporary hairs, it would appear that erosion of the Jane Austen hair occurred after her death. A likely explanation is that the normal saprophytic yeasts remaining on the hair at the death of Jane Austen were starved of their normal supply of nutrients (for example sebum and perspiration) and resorted to a mycelial and mildly invasive form before dying altogether.

I thank the Jane Austen Society for the loan of the lock of hair and Dr A. C. Brown for his help.

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Variation in Lead Concentration along Single Hairs as Measured by Non-Flame Atomic Absorption Spectrophotometry

MEASUREMENT of trace elements in human hair has been used to give, indirectly, answers to several important problems. The detection of clinical poisoning is often indicated by heavy metal buildup, such as Pb, Se, Hg and Tl, in the growing hair¹. Kopito *et al.*² have shown that the detection of lead in hair is a particularly useful diagnostic aid for even mild plumbism. Hair grows at a rate of approximately 1 cm per month, accumulates lead, and thus forms a permanent record of lead content in the body which may be used to estimate the time and length of exposure to lead.

Trace elements in hair may also indicate the environmental level of elements which could possibly be hazardous to health. Hammer *et al.*³ related the As, Cd, Cu, Pb and Zn concentrations in the hair from schoolboys in five cities of known environmental exposure gradients (the major industries in the most contaminated city were lead and zinc mining and smelting; the least contaminated city had education and farm trading as the major industries). They concluded, after taking into consideration the problems of exogenous deposition and endogenous absorption routes, and relationships of hair to body burden, that mean hair levels for As, Cd and Pb accurately reflected community exposures to these metals.

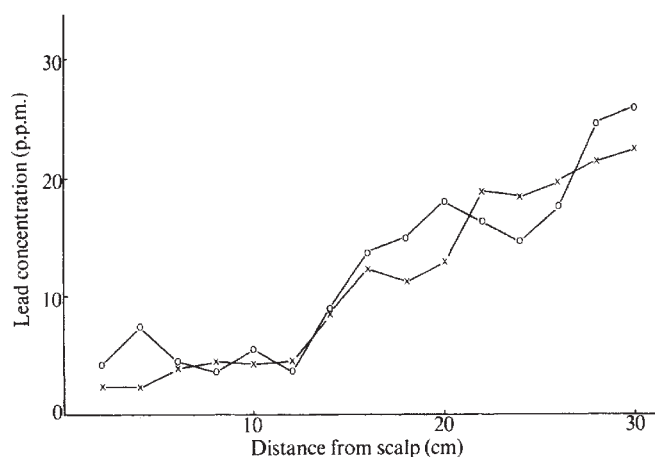


Fig. 1 Lead concentration variation along the length of two different hairs from the same female head. Each data point in the figure represents a lead analysis on the preceding 1 cm section of hair.

It is possible to obtain a detailed record of lead exposure from analysis by non-flame atomic absorption spectrophotometry⁴ on sections of a single hair. Fig. 1 depicts the lead concentration pattern along the length of two different hairs from the same female head. Analyses were performed on a Perkin-Elmer 303 atomic absorption spectrophotometer equipped with an HGA-70 furnace atomizer. The absolute detection limit for lead with this system is 5×10^{-11} g. Before analysis, the hairs were washed by refluxing in diethyl ether in a Soxhlet apparatus. The HGA-70 could be programmed so that the organic material in the hair is removed at a temperature below that at which lead volatilizes. The lead absorption signal was then recorded at 2,400° C in a matter of seconds. Each data point in the figure represents a lead analysis on the preceding 1 cm of hair (approximately 50 µg). The lead concentration is seen to increase significantly from the root to the tip of the hair, suggesting that lead has entered the hair by deposition on its surface followed by diffusion into the hair structure.

By analysing several sections of single hairs from the same head at regular time intervals sudden exposures to lead should be readily detected, especially if a proximal section of the hair shows a sharp increase in lead concentration over its neighbouring section.

Other metals, such as Ti, Zn, Cd, Cu and Fe, may also be monitored in a similar manner.

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Biological Effects on the Early Atmosphere

MANY authors tacitly assume that the presence of life had no significant effects on atmospheric composition until after the appearance of photosynthesis with evolution of oxygen (compare refs. 1 and 2). This assumption seems implausible on biochemical and ecological grounds.

The ancient anaerobic ecological system, as the current aerobic one, must have been in a quasi-steady state: otherwise organic material would have accumulated indefinitely. In the current system, the steady state results from the near equality of the backward and forward rates of the reaction $\text{H}_2\text{O} + \text{CO}_2 \rightleftharpoons (\text{CH}_2\text{O}) + \text{O}_2$. Assuming an anaerobic system and photosynthesis without production of oxygen (say, $2\text{H}_2\text{S} + \text{CO}_2 \rightarrow (\text{CH}_2\text{O}) + \text{H}_2\text{O} + 2\text{S}$, as by some photosynthetic bacteria), the breakdown of organic material would occur, as it does now in the same conditions, by fermentation. In principle, this would return organic material to the state of H_2S and CO_2 . In practice, it is well known that as well as CO_2 , large amounts of volatile organic materials are produced, and also molecular hydrogen; this can be shown by the fermentation of sludge in sewage works and in the anaerobic bottoms of marshes. The composition of the gases evolved varies with conditions and the organisms present, but generally methane is the chief product, hydrogen varying from about 1 to 20% of the methane formed^{3,4} (for a survey of biological hydrogen production see ref. 5). In the steady state, the amounts of such materials produced by fermentation in unit time would closely equal the equivalent amount of organic material produced by photosynthesis.

Thus volatile fermentation products such as methane and molecular hydrogen, as well as smaller amounts of alcohols and other components, would be released into the atmosphere. The steady state quantities present would, of course, depend not only on the rate of release, but also on the efficiency of various sinks, and are therefore difficult to estimate. It is not, however, safe to assume that the quantities would be negligible. An order of magnitude application to the problem of the loss of terrestrial hydrogen into outer space may illustrate this. Urey⁶ has shown that loss of hydrogen would be self-limiting if the hydrogen were produced by ultraviolet photolysis of water: the resulting ozone layer would shield atmospheric water from further effects of ultraviolet light; however, this conclusion might be irrelevant were the ecological system anaerobic, producing hydrogen by fermentation. Brinkmann² estimates that at the present, and presumably also in ancient times, about 1.6×10^9 molecules of water $\text{cm}^2 \text{ s}^{-1}$ dissociate in the atmosphere due to the action of ultraviolet light. This produces 0.8×10^5 tons of atomic hydrogen annually, some of which escapes. The current annual fixation of carbon by photosynthesis is generally believed considerably to exceed 10^{11} tons. Assuming a ratio by weight of carbon to organically bound hydrogen of 5:1, a biological system of this size, operating anaerobically and releasing only 1% of this hydrogen as H_2 , would produce something in excess of 2×10^8 tons of molecular hydrogen annually, or of the order of a thousand-fold more than Brinkmann's estimate. With regard to the probability of escape, a hydrogen molecule would be four times less likely to do so than a hydrogen atom, but the discrepancy in abundance would more than make up for the difference, and also molecular hydrogen itself would be liable to dissociate. Of course the anaerobic ecological system may have been smaller than the present one and the production of hydrogen less. It should be noted, however, that anaerobic metabolism *per se* does not limit the overall size of ecological systems as, both in aerobic and anaerobic situations, the limit is set by energy input from photosynthesis, which is independent of the type of metabolism.

Significant steady state concentrations of fermentation products in the early environment might well have had other important geophysical and biological consequences. Clearly, the effect of biological systems on the atmosphere before significant amounts of oxygen were produced by photosynthesis should be considered when dealing with such matters.

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Mercury in Marine Organisms of the Tay Region

THERE has been increasing concern recently about the quantities of heavy metals, such as mercury, which may accumulate in many organisms. In spite of studies in Japan¹, Sweden²⁻⁴ and North America^{5,6}, concentrations of mercury in populations of marine algae and invertebrates have received little attention, notably in the United Kingdom. Klein and Goldberg⁶ reported average mercury concentrations in epibenthic animals from near La Jolla, California, of 0.9 p.p.m. dry weight with a maximum of 21 p.p.m. in a cowry (*Cypraea* sp.) and values of 0.037 p.p.m. and 0.023 p.p.m. have been recorded in the algae *Laminaria hyperborea* and *Fucus vesiculosus*⁷. We present here data on mercury concentrations which were found in some organisms collected from the Tay region. These vary according to the sampling area examined and are highest in organisms receiving direct discharge from the Tay.

Total mercury was determined by flameless atomic absorption spectrophotometry using an EEL model 240 atomic absorption spectrophotometer fitted with an EEL hollow cathode mercury lamp (lower limit of detection 0.001 µg of mercury). The method used was a modification of that described

by Thorpe⁸ and results are expressed on a wet weight and on a dry weight basis. The expression of mercury concentration on a dry weight basis eliminates variation due to fluctuations in water content which occur particularly in intertidal estuarine areas.

The total mercury concentrations in marine macro-algae and molluscs, collected from the littoral zone at Broughty Ferry in the Tay estuary (national grid ref. NO. 465304) and from an area north of Arbroath (national grid ref. NO. 659410) in October 1971, are presented in Table 1. The sampling areas represent widely differing habitats in that the Broughty Ferry site is subject to the discharge of freshwater from the River Tay, while that north of Arbroath is a fully marine environment. Mercury was determined in each plant species by collecting and pooling at least twelve plants at each sampling, and assaying triplicate 2 g samples of these. The number of replicates in the animal studies varied and these are detailed in the legends to each table.

High levels of mercury were found in the Broughty Ferry algae while there was no detectable mercury in any of the samples collected from north of Arbroath. Most was found in the thallose algae *Ulva lactuca* and *Porphyra umbilicalis*, and in *Ceramium rubrum*. It is not known what proportion of the mercury present was adsorbed on to the surface of the thalli but adsorption of mercury by freshwater algae is reported to be appreciable³. In the studies carried out on molluscs high levels were found in the lamellibranch *Mytilus edulis* and in the gastropods *Littorina littoralis* and *Nucella lapillus*. These species represent three different feeding types; suspension feeders, herbivores and carnivores, respectively. Thus mercury is present at appreciable concentrations at several trophic levels in the Tay estuary.

The distribution of mercury within individual organisms was studied using *Fucus vesiculosus* and *M. edulis* from Broughty Ferry. The results (Table 2) show that in *F. vesiculosus* the highest levels occurred in the stipe and holdfast, and that in the remainder of the thallus there was a gradual increase in concentration toward the apical region. This is seen particularly in the dry weight data. The concentration of mercury in *M. edulis* was greatest in the ctenidia which may represent the principal organs of uptake and release of mercury in this animal. A similar role has been suggested for the gill lamellae of the crustacean, *Maia squinado*⁹, and for the gills of the roach, *Leuciscus rutilus*¹⁰.

Table 1 Mean Total Mercury Concentrations in Algae and Molluscs of the Tay Region

	Broughty Ferry		Arbroath
	µg Hg g ⁻¹ wet weight of tissue	µg Hg g ⁻¹ dry weight of tissue	µg Hg g ⁻¹ wet weight of tissue
Algae			
Chlorophyceae			
<i>Enteromorpha compressa</i> (L.)	0.141	1.007	<0.001
<i>Cladophora rupestris</i> (L.)	0.128	0.826	<0.001
<i>Ulva lactuca</i> L.	6.259	25.537	<0.001
Rhodophyceae			
<i>Polysiphonia lanosa</i> (L.)	0.150	0.612	<0.001
<i>Ceramium rubrum</i> (Huds.)	0.485	3.031	*
<i>Porphyra umbilicalis</i> (L.)	0.506	2.353	<0.001
<i>Rhodomenia palmata</i> (L.)	*	*	<0.001
Phaeophyceae			
<i>Ascophyllum nodosum</i> (L.)	0.067	0.319	<0.001
<i>Fucus serratus</i> L.	0.265	1.153	<0.001
<i>Laminaria digitata</i> (Huds.)	0.131	0.794	<0.001
Molluscs †			
<i>Mytilus edulis</i> L.	0.639	2.112	*
<i>Patella vulgata</i> L.	0.187	0.543	*
<i>Nucella lapillus</i> (L.)	0.480	1.472	*
<i>Littorina littorea</i> (L.)	0.036	0.112	*
<i>Littorina littoralis</i> (L.)	0.564	1.843	*

* No sample collected.

† Each value is the mean from three animals.

Table 2 Distribution of Mercury in *Fucus vesiculosus* and *Mytilus edulis*

Species	Material assayed	µg Hg g ⁻¹ wet weight of tissue	µg Hg g ⁻¹ dry weight of tissue
<i>Fucus vesiculosus</i> L.	Stipe and holdfast	0.096	0.206
	Branches of first dichotomy	0.038	0.083
	Bladders	0.029	0.102
	Sub-terminal branches	0.047	0.130
	Apical tips	0.043	0.143
<i>Mytilus edulis</i> *	Visceral mass	0.275	1.347
	Foot muscle	0.364	0.765
	Mantle	0.871	4.261
	Ctenidia	3.412	19.950

* Each value is the mean obtained from three animals.

Variations of mercury concentrations with time were studied over a 9-day period in December 1971 in *U. lactuca*, *P. umbilicalis*, and in the ctenidia of *M. edulis*. There were appreciable variations with time in all three species which indicate a rapid

accumulation and loss of the metal in these organisms. The percentage variations of mercury concentration with time in the ctenidia of *M. edulis* were less than those in *Ulva* and *Porphyra*, and maximum concentrations occurred 4 days after maximum values were found in the algae. Rapid fluctuations of mercury concentrations in the freshwater alga *Oedogonium* sp., in response to changes in mercury concentration of the water, have also been noted³.

Table 3 Total Mercury Levels in the Eider Duck and the Grey Seal

	$\mu\text{g Hg g}^{-1}$ wet weight	$\mu\text{g Hg g}^{-1}$ dry weight
<i>Somateria mollissima mollissima</i> (male)		
Liver	0.579	2.140
Kidney	0.366	1.825
Adrenal gland	1.219	6.905
Pectoral muscle	<0.001	—
Heart muscle	<0.001	—
Lung	<0.001	—
<i>Halichoerus grypus</i> (female)		
Liver	66.074	224.850
Kidney	4.829	23.507
Spleen	0.700	2.716
Blubber	2.717	3.143
Skin and hair	4.369	8.989

The first species died from an abdominal carcinoma; the second from a fracture of the skull. Each value is the mean of at least three determinations.

Analyses carried out on two vertebrates, *Halichoerus grypus* (the grey seal) and *Somateria mollissima mollissima* (the eider duck) are presented in Table 3. Although analyses were carried out on single animals, it is clear that high levels of mercury were present and were concentrated in the livers and the kidneys of both species. Similar findings have been reported for pheasants (*Phasianus colchicus*) and corvids (*Corvus corone cornix*) which had been found dead in Sweden^{11,12}, although the concentrations of mercury in the livers of these birds (28–140 p.p.m. in pheasants and 29–110 p.p.m. in corvids) were much higher than in the eider duck studied here.

Further studies on heavy metal concentrations in organisms from the Tay region are being undertaken.

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Lead Pollution from a Factory manufacturing Anti-Knock Compounds

IN spite of the present discussion of lead pollution, little attention has been paid to pollution from factories manufacturing anti-knock compounds which consist of tetraethyl and tetramethyl lead. In a study of the edaphic factors affecting certain grassland communities in Cheshire, I found significant levels of lead in vegetation close to such a factory. This prompted a study of the fallout from this factory, which is surrounded by a variety of habitats, including coniferous and deciduous woodland, scrub and agricultural grasslands. The study area was a thin strip of deciduous woodland running approximately due east of the factory; it was largely open birch woodland with a well developed field layer of grass species. Ground layer bryophytes were less well represented; these are good accumulators of airborne metallic elements^{2,4} and Goodman and Roberts⁵ have used epiphytic material of *Hypnum cupressiforme* as an indicator of non-ferrous metals in the air in the Swansea area. Epiphytes are poorly developed in the area of Cheshire studied owing to the sulphur dioxide content of the air (125 $\mu\text{g}/\text{m}^3$ from analysis of epiphyte communities⁶). Because the species composition varied considerably along the transect, no single moss species could be sampled at all sites. Species found in abundance at the sample sites were collected and their mean lead content was taken as a measure of the lead accumulated in the ground layer.

Interspecific differences in lead accumulation may give rise to errors, particularly where ectohydric and endohydric species are concerned. But at sites where three or more species were sampled there was fairly good correspondence in the lead contents of the species. The species used were *Ceratodon purpureus*, *Eurhynchium praelongum*, *Mnium hornum*, *Mnium punctatum* and *Acrocladium cuspidatum*. The field layer was sampled by excising green, healthy leaf blades of *Holcus lanatus*, which is widely distributed in the open woodland and surrounding pastures. Soil samples were taken from the top 2 cm of soil under tussocks of *Holcus lanatus*. Sampling was carried out in the early winter of 1971.

Samples of moss were washed thoroughly in several changes of distilled water to remove soil particles, dried at 60°C, and digested in a 4:1 mixture of nitric and perchloric acids. Leaves of *Holcus lanatus* were dried and digested without previous washing. An acetic acid soluble soil extract was prepared by treating air-dried soil with 0.5 M acetic acid (1:2 by weight) for 5 h at 25°C on a waterbath with shaking. Lead was determined by atomic absorption flame photometry.

Fig. 1 shows that there was a rapid decline in the lead concentration in the vegetation away from the factory in the first 400 m and a slower decline in the next 400 m. At 800 m, however, the amount of lead in the mosses was between two and three times that in the same species collected from rural areas remote from any industry. This suggests that significant concentrations of lead are carried a considerable distance from the factory. This was exemplified by analysis of vegetation close to a major road in central Manchester (Table 1). Samples of *Ceratodon purpureus* and *Holcus lanatus* were taken 2 and 20 m from the road. Values for the 20 m sample were close to the background level of contamination in Manchester, little affected by local roadside contamination. The levels observed in the vegetation 800 m from the factory are very similar to those found as background contamination in central Manchester. Leaves of *Holcus lanatus* were sampled from several

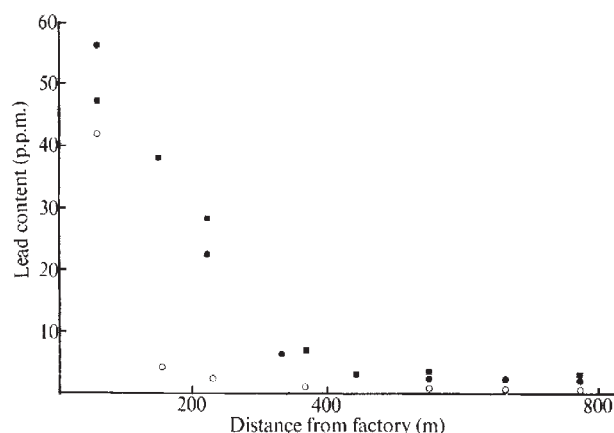


Fig. 1 Mean lead content of plants and soil downwind of the factory. ●, Mosses ($\times 10^{-2}$); ■, *Holcus lanatus* ($\times 10^{-4}$); ○, soil.

pastures which lie within a 400 m radius of the factory. Concentrations as great as 286 p.p.m. were observed in a pasture downwind of the factory: this was nearly three times as much as in roadside samples from central Manchester. Levels of extractable lead in soil were low but showed a similar pattern to those in the vegetation.

Table 1 Lead Content (p.p.m.) of Roadside Plants in Central Manchester

Distance from road (m) Species	Lead content (p.p.m.) 2	$\pm$ s.e. 20
<i>Ceratodon purpureus</i>	320 $\pm$ 12	185 $\pm$ 9
<i>Holcus lanatus</i>	106 $\pm$ 5	37 $\pm$ 2

Large concentrations of lead accumulate in the vegetation immediately around the factory and significant values can be detected in pastures and semi-natural woodland for at least 800 m.

The absolute values observed close to the factory are among the largest recorded. A sample of *Holcus lanatus* from immediately outside the factory had a lead content of 1,838 p.p.m. This is considerably higher than values obtained for grass species^{3,5}. Such large internal concentrations would be expected to be deleterious to growth and therefore to limit primary production, but because the grass samples were not washed before analysis it is impossible to say what proportion has penetrated the leaf cuticle. Although the internal concentrations of lead may be important in limiting primary production, it is total concentrations that are significant for herbivorous species. Some of the contents recorded in *Holcus lanatus* are likely to be highly toxic to herbivores. Small mammals are particularly sensitive to lead poisoning^{7,8}. Care must be taken in interpreting the absolute values observed at one particular time, for there is presumably a seasonal fluctuation in lead content dependent on growth. Mosses grow actively in the autumn and spring so that plants sampled in the early winter should give near minimum values. Grass species would be expected to yield minimal values in the spring and early summer and maximal values in the winter, on the assumption that little lead is absorbed from the soil⁹.

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Population Differentiation in *Marchantia polymorpha* L. in Various Lead Pollution Levels

SURVEYS of heavy metal pollution using bryophytes have produced valuable information about lead levels in the environment. *Hypnum cupressiforme* Hedw., *Hylocomium splendens* (Hedw.) B. and S., *Pleurozium schreberi* (Brid.) Mitt., and *Sphagnum magellanicum* Brid. have been used to demonstrate regional gradients of lead and other non-ferrous metals in Sweden¹⁻⁴, and high levels of lead and other metals have been found in *Hypnum cupressiforme* downwind from the Swansea urban industrial complex⁵. Centres of large urban areas, where pollution-sensitive pleurocarpous mosses are absent but where high levels of lead might be expected, have not been studied.

I report here a preliminary study of lead levels in populations of the liverwort *Marchantia polymorpha* L. which is relatively common in moist shady streets in the centre of Glasgow and Edinburgh and is also found in country districts. Eleven of the samples were collected along a transect running approximately north-west from central Glasgow to a point 13 km from the city. I report also the results of experiments on the lead tolerance of *Marchantia* clones in which plants from high and low risk areas were collected and grown on lead-containing media to investigate genetic variation in lead tolerance in relation to the magnitude of lead pollution in natural habitats.

Samples of *Marchantia* and the soil (1–2 cm) beneath them were collected in polythene bags and dried naturally. Soils were sieved (144 mesh cm⁻²). Thalli of *Marchantia* were washed for two minutes in demineralized water to remove dust and soil particles, and all samples were dried at 100° C. Plant material was digested for 6–8 h at 180°–200° C in specially purified concentrated nitric acid; soil samples were shaken for 1 h in 0.5 M 'Analar' acetic acid. The lead content of plant digests and soil extracts was determined by atomic absorption spectrophotometry (air/acetylene flame); every precaution against contamination was taken.

High lead levels were found in *Marchantia* and in soils from the centres of Glasgow and Edinburgh (Table 1), and in samples from Chatsworth, Dunoon and Beattock which are away from large urban areas but near roads. Samples taken at different distances from the centre of Glasgow suggest that there is considerable lead pollution in the west end of the city and near main roads in Bearsden, but lower levels were found 10–13 km NW of the city, in the Milngavie area, especially away from roadways.

Lead levels in the liverwort show no constant relationship to the lead content of the upper 1–2 cm of the soil, and the following trends are suggested: first, there is usually a greater concentration of lead in the liverwort than in the soil; whether this is due to uptake of the metal from the soil, or due to airborne lead, or both, is not known. Second, high levels of lead in the *Marchantia* thalli are usually associated with high lead values in the soil. An important factor affecting the soil lead level is disturbance; *Marchantia* grows in pockets of city dust or in shallow unstructured soils, which are often disturbed by road and building operations, street sweeping, and heavy runoff of rainwater. In situations of infrequent disturbance,

especially where decaying *Marchantia* thalli are found in the upper soil, high lead values have been found.

Table 1 Lead Levels (expressed as p.p.m. dry weight) in Washed Thalli and Soils in a Series of *Marchantia polymorpha* Populations

Sample sites	<i>Marchantia</i>	Soil	Ratio lead in thallus/soil	Distance from roads (m)
Glasgow region				
1. St Enoch's Square (0)*	5,333	973	5.48 : 1	0
2. Sauchiehall Lane (1.6)	3,858	193	19.98 : 1	0
3. Cromwell Lane (1.6)	2,679	401	6.68 : 1	0
4. Charing Cross (1.6)	1,647	64	25.73 : 1	0
5. University Gardens (2.6)	1,869	252	7.41 : 1	2
6. University East Courtyard (2.6)	1,759	898	1.95 : 1	10
7. Norval Street (3.0)	3,381	463	7.30 : 1	0
8. Garscube Research Labs., Bearsden (6.5)	1,344	475	2.82 : 1	30
9. Milngavie Lime Dumps (10)	398	28	14.21 : 1	20
10. Milngavie Mill Site (10)	150	32	4.68 : 1	50
11. Milngavie Mugdock Castle Ruin (13)	107	129	0.82 : 1	800
12. Dunoon Roadside Town Centre (45 NNW)	5,289	565	9.36 : 1	0
13. Beattock A74 (70 SE)	7,792	1,263	6.16 : 1	0
Edinburgh City Centre				
1. James Court (behind Royal Mile)	767	761	1.01 : 1	10
2. Young Street Lane	1,898	989	1.91 : 1	0
3. Charlton Street	852	269	3.16 : 1	0
Chatsworth Park (track behind car park) Bakewell, England	4,214	353	11.93 : 1	30

* Distance (km) from the city centre is given for specimens collected in the Glasgow region.

Sample sites numbered 1–11 are all approximately north-west of the centre of Glasgow.

Table 1 shows that *Marchantia polymorpha* populations grow in habitats subject to different levels of lead pollution. Four populations were studied to see if plants are differentially sensitive to lead in the medium. *Marchantia* is a dioecious species and sexual reproduction is frequently successful in large undisturbed populations, but single sex colonies, reproducing vegetatively, by means of genetically identical gemmae, are common in cities. As asexual reproduction is common in *Marchantia*, especially in city populations, a single clone from each of the four populations was tested for lead tolerance.

Gemmae, thoroughly washed in sterile demineralized water, were grown in Knop's agar containing either 400 p.p.m. lead (as lead nitrate) or control plates containing no lead, but with sodium nitrate at an equivalent nitrate level. Gemmae were selected at random from the washed samples and five from each clone were placed on each plate. Five replicates of control and lead treatment were prepared. The dishes were placed in a randomized block under strip lights, at an illumination level of 16 lux. The plates were maintained at room temperature ($22^{\circ} \pm 3^{\circ} \text{C}$) in 24 h photoperiods. Growth increments in the maximum length of the developing gemmings were recorded photographically for seven days. No statistically significant difference between replicates within treatments was found (Table 2).

All clones can grow on a medium containing a high level of lead. The three city clones grow equally well on lead agar and control medium (mean values not statistically significantly different), but the Milngavie plants grow significantly less well on lead agar in comparison with the control. This experiment, in which four clones were tested under comparable conditions,

provides clear evidence of genetic difference in lead tolerance: the three city clones, which are subject to high lead pollution in their native habitats, are all highly tolerant of lead, but the Milngavie plants, which grow in an area exposed to less lead contamination, appear to be more sensitive to lead. Further experiments are required, but it seems likely that lead tolerant genotypes have a selective advantage in city regions. When further data are available, lead tolerance in *Marchantia* may be seen as a further example of natural selection operating in an urban industrial environment⁶.

Table 2 Mean Growth Increments in Length (mm) of *Marchantia polymorpha* Gemmings on Lead Agar

Location of clones	Control	400 p.p.m. lead	P
University Gardens*	29.191 $\pm$ 0.726	28.306 $\pm$ 0.755	NS†
University East Courtyard	26.612 $\pm$ 1.014	26.729 $\pm$ 1.587	NS
Cromwell Lane	27.788 $\pm$ 0.978	28.259 $\pm$ 0.905	NS
Milngavie Lime Dumps	28.282 $\pm$ 0.795	23.294 $\pm$ 1.228	<0.01

* See Table 1 for lead levels in natural habitats and parent thalli.

† Not significant.

The mosses *Bryum argenteum* Hedw. and *Funaria hygrometrica* Hedw. are often found in the same habitat as *Marchantia polymorpha*, and I have found (unpublished data) that they too have high lead levels in their tissues. Growing with these bryophytes are common weeds such as *Poa annua* L. and *Senecio vulgaris* L., seeds of which germinate in lead-rich soil; it seems possible that many species of plants found in cities have some degree of lead tolerance which may be physiologically different from that shown by leadmine plants⁷. Plants in urban areas may be subject to greater aerial lead pollution than those on mine debris.

In conclusion, *Marchantia polymorpha*, which I have shown to contain higher lead levels than the bryophytes used in previous studies^{1–5}, could perhaps be a valuable indicator species. Large quantities of liverwort thalli could be grown quickly from gemmae in a pollution-controlled atmosphere in the laboratory, and later exposed in selected sites to study the levels of lead pollution. A pilot investigation is in progress to assess the practical aspects of using *Marchantia* as a sensor.

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Aerial Pollution and the Rapid Evolution of Copper Tolerance

THE geographical spread of aerially borne metals has been demonstrated by analysis of vegetative uptake and accumulation of metallic elements^{1–5}. Because these metals can be extremely toxic to plants in low concentration such aerial

pollution, which is often of recent origin, may be causing significant changes in the genetic structure of the plant populations exposed to them. Metal tolerance in plant populations growing on mines waste is already well known⁶.

A metal refining industry in SW Lancashire was established about 1900. Copper is the chief constituent of the dust particles that have been emitted. Although steps have recently been taken to reduce emission the accumulated soil contamination is now very high, and the grassland near the refinery now has total soil copper levels of up to 4,000 p.p.m.; in some places the vegetation has been totally destroyed. The maintenance of lawns in the immediate vicinity of the refinery has usually depended on the surface soil being changed at regular intervals. Such established grassland as exists is dominated by *Agrostis stolonifera* or sometimes *Agrostis tenuis* and few, if any, other species. The plant community is reminiscent of that to be found on metal contaminated soils of old mine workings.

Within these lawns very different population structures of *A. stolonifera* can be seen. In lawns established within the past 10 yr on ground which is seriously contaminated there is much bare ground; plants are found scattered as individual patches. But in the older grassland in highly contaminated areas the grass is growing well and forms a continuous cover. The metal levels are so high that it seems likely that normal plants cannot grow in these areas. Perhaps tolerant plants formed by mutation or segregation could have been selected and have spread out to form the populations.

Table 1 Characteristics of Sampling Sites

Site	Age (yr)	Soil pH	Total copper (p.p.m.)	Available copper (p.p.m.)	Plant cover	Other species
Normal						
Freshfield dune grassland	—	7.4	33	0.7	Continuous	Many
Sefton Park	—	6.5	66	0.7	Continuous	Many
Refinery						
Boundary grassland	4	4.9	1,930	12	Fairly continuous	Several
New lawn on old flowerbed	8	5.1	4,830	20	Isolated patches	None
Canteen lawn	14	5.3	2,630	19	Coalesced patches	<i>A. tenuis</i> only
Old lawn	70	6.6	4,260	17	Continuous	<i>A. tenuis</i> only

We measured the copper tolerances of 30 individual genotypes of each of four populations of *A. stolonifera* from the refining area and two populations from uncontaminated grassland (Table 1) by the method of McNeilly and Bradshaw⁷. For each genotype ten tillers of comparable size and age were suspended in 300 ml. plastic beakers in a solution containing calcium nitrate at 0.5 g l.⁻¹ and a further ten in a solution containing calcium nitrate and copper as copper sulphate at 0.126 p.p.m., at 21° C and under 24 h illumination.

Marked copper tolerance of different degree in different genotypes was found in the populations (Fig. 1). Its distribution in the six populations (Fig. 2) indicates that the copper tolerances of the Freshfield and Sefton Park populations are uniformly low. In the population on the boundary of the refinery area there is a considerable increase in the occurrence of tolerance, yet this population is more or less continuously distributed and there are several other species; this supports the idea that selection of different genotypes for copper tolerance from an original non-tolerant population is only occurring now. This area has suffered pollution only recently, because a new refinery has been built next to it. In the flower bed, canteen and old lawn populations there is a further progressive increase in the mean copper tolerance and the

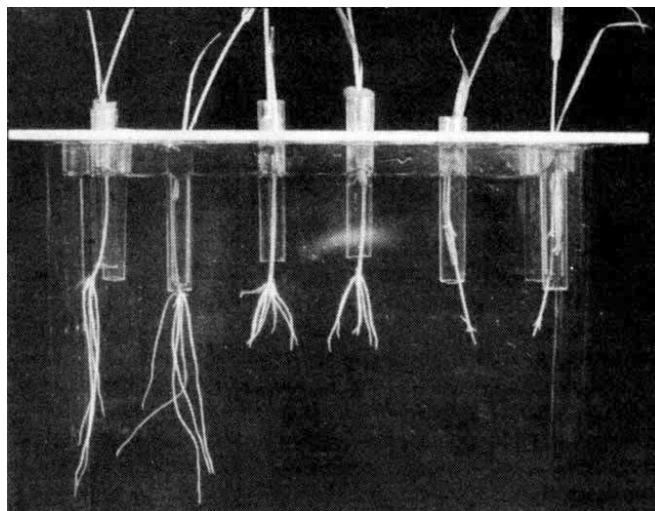


Fig. 1 Root growth of *Agrostis stolonifera* genotypes from refinery area (left and middle) and sand dune (right) grown in copper (0.126 p.p.m.) solution.

disappearance of non-tolerant and slightly tolerant individuals.

Because there are very high levels of copper in the soil at these three sites, all species except *A. tenuis* have disappeared, and they form a series of increasing age and plant cover, it seems reasonable to us that they represent a historic series, in which all individual genotypes except those which are tolerant have been eliminated and the tolerant genotypes have been spreading to close the sward. Because there is an increase in mean tolerance there must also be progressive selection for increasingly tolerant genotypes, perhaps produced by recombination from the original selected individuals.

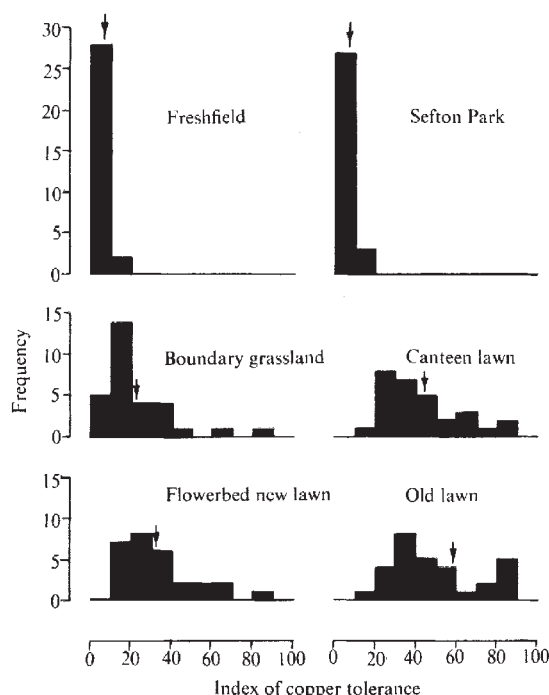


Fig. 2 Distribution of copper tolerance in populations of *Agrostis stolonifera* (population details given in Table 1).

The use of experiments in which seed samples are sown on contaminated soil has been shown to be a sensitive test for the occurrence of metal tolerance and as a demonstration of the power of selection⁷. We therefore collected seeds from the

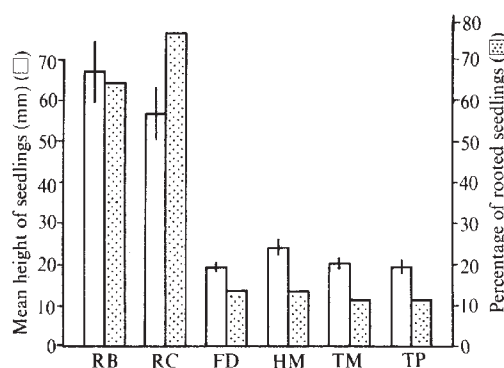


Fig. 3 Seedling height and percentage of rooted seedlings in seed samples on copper contaminated soil after ten weeks growth. (Sample details given in text.)

following sites: Freshfield dune grassland (FD); Trelogan zinc and lead mine (TM); Trelogan normal pasture (TP); Halkyn Mountain lead mine (HM); boundary grassland at refinery (RB); grassland near canteen at refinery (RC). The seeds were sown on toxic soil from the refinery containing 10,260 p.p.m. Cu. After ten weeks, mean height and percentage of rooted seedlings were determined in samples of 2,000 seeds for each population.

The results show (Fig. 3) that there is no difference in the height and the percentage of rooted seedlings between the four seed populations collected from sites not contaminated by copper, including mine workings, when grown on the refinery soil; but there is a significant increase in the mean height and the percentage of rooted seedlings in the two refinery populations. Because these results match the results of the tiller tolerance test they imply a high level of inheritable copper tolerance in the refinery populations. The Trelogan and Halkyn mine populations are known to be tolerant to zinc and lead, and lead, respectively. The results are further demonstration of the specificity of metal tolerance.

The behaviour of the populations in these experiments from the sites uncontaminated with copper is interesting. Although most seedlings have died, there are few which are surviving well. From other work⁹ it is certain that they will be tolerant, and can give rise to a tolerant subsequent generation. Selection for copper tolerance can obviously occur easily.

These results demonstrate evolution in plants in relation to aerial pollution analogous to that found in insects¹⁰. The particular interest is that this evolution must be of very recent origin, and still be in the process of occurring especially in the flower bed population. The process of change and the genotypic structure of the populations are being investigated further.

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Normal IQ Distributions of Early-treated Phenylketonuric Children and their Unaffected Siblings: Failure to Replicate a Trimodal Response or Negative Skew

PHENYLKETONURIA, an inherited metabolic disorder associated with mental retardation, has been generally considered a single gene defect. Fuller and Schuman¹, however, have argued for a more complex genetic model, citing a trimodal frequency distribution of IQ scores for a sample of treated phenylketonurics (PKUs) and a negative skew in the IQ distributions of unaffected siblings as evidence for their model. We have analysed data collected by Hudson² to test the basis of Fuller's findings. Evidence was found for neither a trimodal response to treatment of phenylketonuria nor a negative skew in the IQ distribution of their unaffected siblings. Both groups showed IQ distributions which were not significantly different from the expected, normal, curve for that sample.

The trimodal frequency distribution of IQs reported by Fuller and Schuman¹ represented 110 early and late-treated PKUs. The distribution differed significantly from the appropriate, expected, normal curve with modal points at 30, 50 and 80 IQ. These findings were interpreted as reflecting three different biological populations, with the three modes representing differential responses to treatment. Degrees of dietary control or differences in treatment were interpreted as not affecting the IQ distribution. Furthermore, this interpretation was offered as a possible explanation for "different findings of success or failure of dietary treatment". The data reported were drawn from both early- and late-treated cases; early-treated children were represented only in the upper two modes, but the model proposes that a sufficiently large sample of such children would be distributed trimodally. The first part of our study presents additional data on the IQ distribution of early-treated cases.

The second object of this report is to present additional data on the intellectual status of unaffected siblings of PKU children. Fuller³ reported a negative skew in the IQ distribution of her unaffected siblings. Additional data on this issue are important because of the frequent practice of comparing IQs of unaffected siblings with their treated PKU siblings. If the siblings in PKU families are brighter than populations not selected on the basis of phenylketonuria, the sibling comparisons may be misleading.

The IQs of the early-treated children used in this analysis were all obtained from Hudson's report². All cases were identified on the basis of biochemical evidence, and treatment was begun before the age of 4 months. Hudson collected the information from the following sources: 15 from the Liverpool series; 48 from the PKU Register, Medical Research Council (United Kingdom); 58 from the PKU Registry, Hereditary Defects Unit (State of California Department of Public Health); and 63 from the literature, including 7 cases from the Children's Hospital Research Foundation in Cincinnati. Hudson was careful not to duplicate cases and there is no overlap between the cases reported by Hudson and by Fuller³.

Only cases on diet at time of last testing and tested with the Stanford-Binet Intelligence Scale (>2 years old) were included for analysis in the present study. Sixty-one cases of the total 184 early-treated cases met the above criteria.

The IQs of normal or unaffected siblings of PKU children analysed were also taken from Hudson's table. Seventy IQs were available.

Hudson's IQ scores on 61 cases ($\bar{X}$ IQ=96, s.d.=16) were subjected to χ^2 analysis with 0.5 sigma units defining the intervals. The observed IQ distribution for the 61 cases does not differ significantly from the expected normal curve with the same number of cases ($\chi^2 = 9.14$, df = 5; $0.25 > P > 0.10$). Frequency distributions of IQs for Hudson's early-treated cases and for Fuller's 26 early-treated cases⁴ are shown in Fig. 1. The combined distributions for both sets of data (N=87) are also

shown. Clearly, the mode at IQ 60 described by Fuller is still apparent in the combined distribution, because none of Hudson's cases fell in IQ range below 65. The apparent bimodal distribution of the 26 cases diminishes considerably when combined with the data of our study.

As noted by McNemar⁵, the mode is highly susceptible to sampling error as a function of sample size. If a given variable is normally distributed, increasing the sample size should lead to closer approximations of the bell curve. This should, of course, not occur if, as Fuller maintains, the three modes represent biologically different populations. It is clear that the results presented here do not support the hypothesis with early-treated cases.

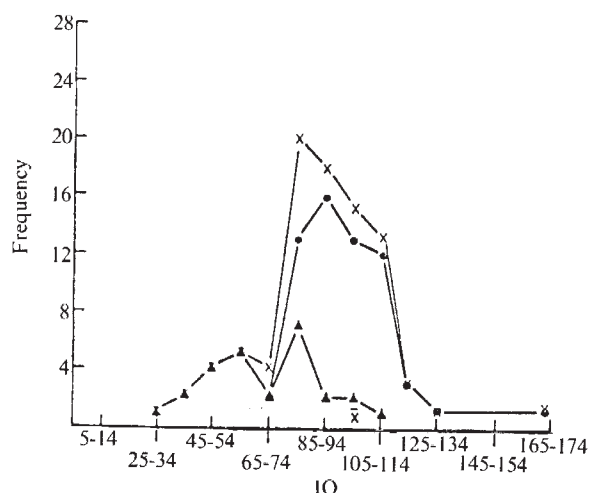


Fig. 1 Frequency distributions of IQs of early-treated PKU children: ▲, IQ distribution of Fuller's 26 early-treated cases; ●, IQ distribution of Hudson's 61 early-treated cases; X, distribution of pooled IQ scores (N=87).

Furthermore, the clear difference in mean IQ score between the early-treated groups may reflect the different criteria of early treatment. Although the exact scores of Fuller's cases were not available, a mean IQ can be estimated using the midpoint of the 9 point IQ intervals⁴. Such an estimate yields a value of 69 for her early-treated cases, compared with a mean IQ of 96 for Hudson's 61 early-treated cases. Fuller used 6 months old as the criterion for early treatment; but this may not be an appropriate period. Baumeister⁶ showed that while 45% of children treated at less than 15 weeks old had IQ scores of 90 or greater, only 14% of those treated from 20 to 52 weeks had IQ scores in this range. In our study children treated before 4 months old were termed early-treated.

The failure to confirm Fuller's results in early-treated cases casts some doubt on the trimodal theory as a whole. Although it is clear that her results are trimodal, the distribution may be viewed as a partial result of pooling early and late-treated cases. It is also noteworthy that, in the original trimodal distribution of IQ scores for 110 cases, the upper mode (IQ 80-90) is mainly due to the early-treated cases, and removal of these leaves a distribution approaching bimodality. This remaining bimodal distribution (IQ 30 and IQ 50) may partially reflect an artefact of measurement, that is, the lower mode (IQ 30) may represent a floor effect on the Binet scale which artificially inflates the IQ interval between 25-34; for example, any child between the ages of 10 years 0 months and 8 years 3 months with a mental age of 2 years 6 months would receive an IQ of 30.

This study also examined whether the unaffected siblings reported by Hudson showed exceptional brightness on IQ tests compared to a hypothetical population with a mean IQ of 100 and an s.d. of 16 (Binet mean IQ and s.d.). Fig. 2 shows the observed IQ distribution of 70 unaffected siblings, and the normal curve for the same number of scores with a mean IQ of 100 and standard deviation of 16. The actual mean IQ is

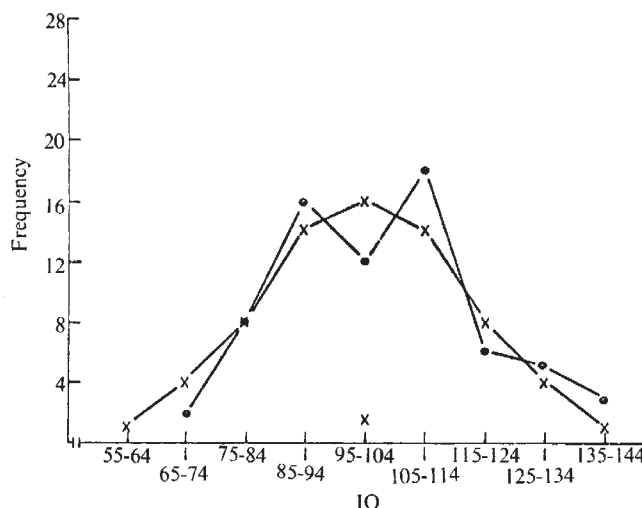


Fig. 2 Frequency distributions of IQs of the normal siblings of PKU children: ●, observed IQ distribution of 70 normal siblings; X, expected IQ distribution of 70 cases with mean of 100 and s.d. of 16.

103, with a standard deviation of 17. Chi-square best-fit was used to analyse the data. The observed IQ distribution of the 70 unaffected siblings does not differ significantly from the expected normal distribution with the same number of cases ($\chi^2 = 7.69$, $df = 6$, $0.25 > P > 0.10$).

It should be noted that the report by Munro⁷, cited by Fuller as earlier evidence of either a negative skew or a higher percentage of IQs in the high IQ ranges for unaffected siblings, appears to have been misinterpreted. Munro was comparing sibs in PKU families with sibs in families with moderately and severely retarded children (non-PKU). The data suggested a single genetic factor determining low intelligence in the PKU cases, as opposed to multifactorially-determined low intelligence expected on the basis of familial mental retardation. Thus Munro's data have little bearing on the question of exceptional brightness in unaffected siblings by comparison with the normal population.

In summary, our data indicate normal IQ distributions in the early-treated PKU cases and unaffected siblings. These data are consistent with a single gene defect in phenylketonuria and question the more complex model hypothesized by Fuller and Schuman¹.

This work was supported by grants from the US Public Health Service, National Institute of Child Health and Human Development, the National Foundation, and the Maternal and Child Health Service, Health Services and Mental Health Administration.

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BOOK REVIEWS

Nuclear Power

Nuclear Energy Today and Tomorrow. By D. Z. Robinson, C. B. A. McCusker, P. W. McDaniel, W. K. H. Panofsky and R. H. Dalitz. Pp. 473. (Heinemann: London and Edinburgh, September 1971.) £3.25.

THIS book is a compilation of many lectures given in Sydney to the Twelfth International Science School for High School Students. Some of the students were sent by the USA and Japan and some were sent by the Royal Institution; the lectures were intended for the layman also. They cover a wide field of nuclear science and technology ranging from cosmic rays, the elementary particles and nuclear forces to nuclear power and the use of radioactive isotopes. Readers will find in the compass of 400 pages a vast amount of information dealing with developments on the frontiers of science.

The first two chapters on science and society by an American professor start, alas, on the wrong foot for students: we learn on the first page that King Charles II set up the Royal Observatory of Greenwich in 1714 and in the same year Parliament offered £20,000 for the invention of a device for the accurate determination of longitude. It is also unfortunate for students that these chapters deal only with the American scene and the lecturer believes "that other countries are trying to change their structures to more closely approach the American model", apparently unaware of such structures as the British DSIR, which started at the end of the First World War, and the other research councils which have been employing scientists and advising policy makers for a very long time. He tells these young students that "science will advance only through the use of expensive tools", a most misleading assessment ignoring the discovery of the double helix, the laser, and holography, the products of clever thinking, not expensive tools.

There are five chapters on the peaceful uses of the atom. The first deals with the multifarious uses of isotopes and radiation and covers the ground

very thoroughly: it is unfortunate that it contains errors of basic science which some of the students could no doubt have corrected, for example Rutherford described the properties of the alpha and beta particles before he left Cambridge for Montreal; Soddy was not working with him at that time; nor did Soddy help him in the identification of the alpha particle with the charged nucleus of a helium atom; the nucleus was not born till Rutherford was in Manchester; and Rutherford had no colleagues when he first observed the transmutation of nitrogen into oxygen in 1919. It is surprising that there is no mention of Fermi's work in Rome on the production of artificial radioactivity by neutron bombardment enhanced when the neutrons have been reduced to low velocity. For this work he gained the Nobel Prize and it is basic to the development of the nuclear reactor described in the following chapter. This second chapter is *not* headed "American Nuclear Power Development", yet it deals exclusively with the American scene and gives no account of the first nuclear reactor for the generation of a significant amount of electricity, the Russian reactor described in 1955, nor of the huge British developments which, as many schoolboys know, have produced more electrical units of power than have been produced in any other country. To remove heat from a reactor core we are told "Materials such as liquid metals, organic liquids, fused salts, high pressure water, etc., are used", but there is no mention of carbon dioxide which has removed far more heat from reactors than has been removed by any other substance: the chapter is a very unbalanced account to present to students from several countries and to the lay audience in Sydney. Incidentally "On December 2, 1942, scientists under the leadership of Enrico Fermi, an American of Italian origin, for the first time in history produced a self-maintaining chain reaction"; they did, but Fermi then was an Italian and had to wait another 19 months before he became an American.

The chapters on the use of nuclear energy for space travel and for large

industrial projects make very interesting reading but there is no reference to the amount of radioactivity left on the ground when nuclear explosives are used for creating huge trenches; perhaps the information was not available when the lecture was given so we do not know whether there is any future for such earth-moving projects. The fifth chapter, on thermonuclear reactions, only lists American work, ignoring the British and Russian contributions, the neutrons described by Kurchatov in 1956, and the neutrons produced in "Zeta" and "Sceptre" before those in the American "Scilla" which he describes as the "first laboratory thermonuclear plasma produced in 1958". Surely a lecturer to an international group of students ought to present an accurate account, and if possible, a comprehensive account of his subject.

In the second half of the book a better balance is preserved. The chapter on cosmic rays tells the exciting story on a world-wide basis from the earliest discoveries in 1910 to the latest which reveals particles with energy of 10^{20} electron volts. Professor Panofsky explains why we need the big machines to further the "25-century old quest to understand the ultimate constitution of matter"; he describes all the important developments from the original small cyclotron of 1930 to the two-mile-long lineac and half-mile diameter accelerators now being built, and finishes with a glimpse into the future when colliding beams may be used and when magnets may be created by superconducting windings to open up a vast new field of endeavour. Interspersed with his lectures were those of Professor Dalitz on the huge family of "new particles", now more than 200 of them, though "there are very few of us today who feel that there is anything elementary or fundamental about any of them". His lectures on symmetries and selection rules, the new spectroscopy, and the weak decay interactions are masterpieces of erudition but I wondered whether they were capable of being appreciated by boys just finishing school; they would be very suitable for research students or

honours physics undergraduates in their final year. His final lecture on "Open Questions" must have been most impressive. "How little we understand about this field of physics"; maybe the next decade, with the help of the new machines, will reduce the plethora of particles to just a few "quarks".

T. E. ALLIBONE

Ancient Fish

Palaeozoic Fishes. By J. A. Moy-Thomas. Second edition extensively revised by R. S. Miles. Pp. xi+259. (Chapman and Hall: London, 1971.) £4.25.

THE original *Palaeozoic Fishes* (1939) aimed to present the latest research on the early history of fishes to zoology and geology students and in this it succeeded. Because most significant fish evolution was accomplished or initiated in the Palaeozoic, it formed a most useful little book for many years. With publication of this revised edition, the aim has again been admirably fulfilled. The first edition had long been seriously out of date so that revision was no small task, and the text has indeed been largely rewritten. As before, the

arrangement is systematic, but among other improvements references are now incorporated in the text and the modern approach is reflected in new sections such as functional morphology and mode of life. The revision is thorough, controversial areas are covered briefly but fairly and the balance of the original is maintained. The result is an enjoyable and worthwhile volume, filling the gap in the literature of vertebrate palaeontology left by its predecessor. This work is much larger than the first but equally compendious, and the increase therefore only indicates growth of the subject. The new format has allowed a far better set of illustrations than before: they are uniform in style, clear and clearly labelled, although with such wide choice it seems a pity that the cover drawing is one described within as "known to be incorrect". The price is inevitably higher, but should not deter anyone interested in the field.

It is unfortunate that so fine a work contains numerous misprints. Most really disturbing examples have been corrected by an erratum slip, but others remain, some of them rather misleading. For instance, in comparing branchial arches in chondrichthyans and osteichthyans "<-shaped" and ">-shaped" are transposed and refer to the wrong groups, while antiarchs are stated not to

exceed 30 mm in length, a figure too small by a factor of ten.

These minor points do not undermine the book's value, and it will surely be welcomed by postgraduates and teachers as well as students whose curricula include vertebrate palaeontology. If it is now taught to this level less widely than in 1939, it could be argued that the need for a way into this interesting subject is greater. It is in the nature of this type of book to go out of date relatively quickly, but I hope it can be revised at more frequent intervals in future.

S. M. ANDREWS

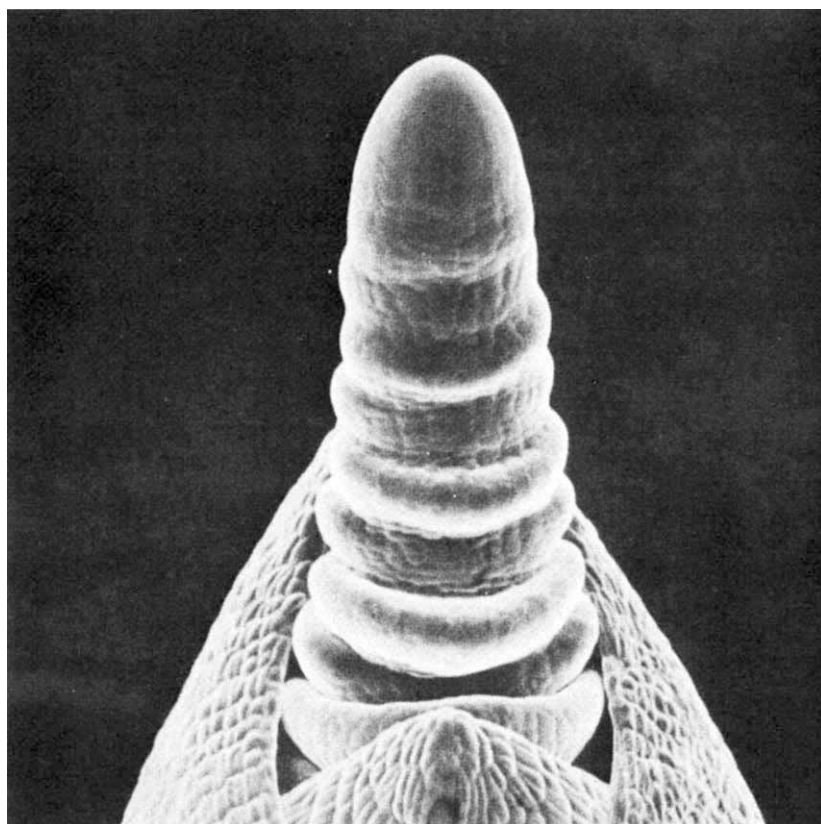
Describing Vegetation

Description and Classification of Vegetation. By David W. Shimwell. Pp. xiv+322. (Sidgwick and Jackson: London, March 1972.) £2.25 paperback; £5 cloth.

DR SHIMWELL hopes that his book will provide a basic manual for ecologists of the various methods of describing vegetation. His timely review is valuable for its clear account of the Zurich-Montpellier and other schools of phytosociology.

The first chapter covers quadrat sampling and statistical methods, subjects explained more fully and far more accurately elsewhere. Students should be dissuaded from reading this confusing summary. Chapter two describes the history of concepts like "formation" and "association" and might well have been left out. The style and presentation of the rest of the text are of a higher standard. Non-floristic features of vegetation which have been used in classification are dealt with in the third chapter, which contains a lucid account of Raunkiaerian life-forms and their applications. Excellent discussions of succession, the nature of the climax, pattern and process and van Leeuwen's relation theory are followed in chapters five and six by descriptions of structural-functional and floristic methods of classification, including a thirty-page account of the Zurich-Montpellier system. After a summary of gradient analysis, continuum analysis and multivariate methods the book ends with some comments on the uses of vegetation description.

Throughout the text the author promotes rapid comprehension of each method and concept by using original examples from species and communities familiar to British ecologists. In some chapters, related techniques are easily compared because they have all been applied to the same data set. Nevertheless, adequate critical comparisons are absent. The shortcomings of the methods and the assumptions under-



The apical meristem of *Arawa* wheat: Plate 69 from *Probing Plant Structure*, by John Toughton and Lesley A. Donaldson (Chapman and Hall, London, 1972; price £1.75). The book contains 105 scanning electron micrographs with captions describing the relation of the anatomical structure to the physiology of the plant.

lying them are rarely mentioned. Beginners have no basis for distinguishing techniques little used in the past from methods commonly used at present. Practical advice is also lacking; for example, those starting to use the Zurich-Montpelier system are not told what proportion of the total ground area might be covered by identifiable associations, or how to recognize and sample fragments, transitions, and communities undergoing succession.

Thus the author has sacrificed detailed analysis to superficial coverage of the whole subject, and the book sometimes reads like a catalogue. In spite of this, parts of the text may be useful to undergraduates and postgraduates as background reading, as an introduction to the literature, especially the continental literature, or in choosing suitable methods for describing vegetation and analysing the results. T. J. KING

Biological Systems

Annual Review of Ecology and Systematics. Vol. 2. Edited by R. F. Johnston. In association with P. W. Frank and C. C. Michener. Pp. ix+510. (Annual Reviews: Palo Alto, California, 1971.)

ONE-THIRD of the reviews in this volume are good and most of the others are useful. In the first, Ayres and Kneese discuss the possibility of a stationary economy and show that in the United States the present problem of the use of material and the generation of waste is due not to population growth but to the increase in productivity. They accept the present UN projections of population growth and suggest four forms of solution, to estimate social costs, to develop technologies which conserve materials and energy, to develop clusters of small cities and to reduce the population growth rate to zero in such a way that the best age distribution is obtained. They extend their arguments to a period of more than 60 years ahead and argue the consequences of a stable population of $1.5-2.0 \times 10^{10}$. It is a most interesting review and doomwatchers should read it.

Theories of feeding strategy are reviewed by Schoener. These are based on time spent feeding, with or without search, in terms of metabolic cost to growth or survival benefit. Any animal has to maximize its future reproductive output in face of its deficit in time spent feeding and searching. There are a number of solutions to such a problem, for example, time minimization and energy minimization. There are specialist and generalist feeders and large animals are probably more effi-

cient than small ones. Several models of feeding and predation are described, leading to the idea of an optional foraging space, a quantitative basis to the concept of territory. This article should be read by ecological model makers.

The tricky problems of river biology have been overcome to some extent by the use of laboratory streams, or fluvaria. Warren and Davis have studied the production and density dependent growth of a river fish, the sculpin. Growth depends on insect density which itself varies inversely as the biomass of sculpins, so there is density dependence in two parts of the two trophic layered system. Fallor reviews the subject of oceanic turbulence very well and explains all the present arguments on scale and coefficients. He also analyses the Langmuir circulation which seeks to explain windrows on the surface of the sea and shows that it is generated by the ruffling or breaking of wave crests.

There are two difficult papers on numerical taxonomy: the source of difficulty lies partly in terminology and partly in the attempt to express continuous variables in rigid dendrograms. A paper on the biological control of insects notes that eighty-one successful programmes had been completed. Maguire discusses dispersal and colonization of protozoa in small patches of water (phytotelmata) on trees in a tropical forest; the balance of immigration and emigration was disturbed by predatory mosquitoes and no relation was found between diversity and the coefficient of variation in the number of taxa.

These are some of several valuable reviews in what makes on balance a worthwhile volume. D. H. CUSHING

Ethology of Sheep

Mountain Sheep: a Study in Behaviour and Evolution. By Valerius Geist. Pp. xv+383. (University of Chicago: Chicago and London, 1971.) £6.55.

DR GEIST is an excellent naturalist writer drawing his reader into his own enthusiasm for his subject. He reports on an important ethological study of three races of mountain sheep, Dall's, Stone's and Big Horn sheep. He is also one of the pioneers in the study of the evolution of social behaviour. On which aspect of this book to find space to comment upon when praise can be so deservedly given to all?

The evolution of social behaviour is, of course, the most interesting and contentious topic discussed in *Mountain Sheep*. Dr Geist adopts the evidence

of a geographic and evolutionary cline among the races of mountain sheep and a comparison of their morphology and behaviour as the basis of his powerful argument.

The flaw I find in his argument is that Dr Geist does not find a place in it for a consideration of the significance of differing sizes of home range groups among different races of sheep. Comparative data are lacking and it can also be agreed that the adaptive value of varying size of group requires proof. Nevertheless, I would suggest that as the primary productivity of the habitat varies so must the size of the home range group or the content of its range, or both, if the sheep are to adapt successfully to the environment and to colonize new areas.

In future editions Dr Geist may care to discuss this point, and I would also be glad to read a more detailed treatment of the interesting attempts to re-establish mountain sheep in various localities.

This is a well-written, interesting book, excellently produced with outstanding photographs.

R. F. HUNTER

Deformation and Flow

Advanced Rheology. By Markus Reiner. Pp. xiv+374. (H. K. Lewis: London, 1971.) £8.

PROFESSOR REINER, by his many published papers and books and by his lectures to international audiences spread over many years, has done as much as anyone to make rheology a respectable branch of physics. His latest work, which he describes in his preface as an essay at a textbook, is valuable in placing on record in one place his account of the historical development of the subject, and his perspective view of the basic concepts that the theoretical rheologist needs to have formulated in mathematical terms.

Except for a short final chapter on elementary structural theories (micro-rheology), the book is mainly concerned with equations of state describing idealized materials on which macrorheological theories can be based. The author shows what is now regarded as an excessive zeal for spring-dashpot models of some complexity, and for the laborious derivation of linear differential equations from them. He permits himself the non-rigorous rectangular-box type of argument to establish fundamental formulae such as the equation of continuity and the stress equations of motion, and the engineer's Mohr-circle diagram to represent a two-dimensional state of stress. He restricts the term

strain to mean what other authors would call recoverable strain, so that it is in general only a part of the deformation of a body. By attaching somewhat more importance than is usual to the particular mathematical measure of a physical concept (deformation, or rate of strain) the author is able to isolate, for separate treatment, linearity, parametric non-linearity, deformational non-linearity and tensorial non-linearity in equations of state.

The deformation and flow situations discussed in any detail are simple ones, for example those in which an element is subjected to an elongational or simple shearing flow. The reader is left to think out for himself what will happen in more complex situations, and perhaps the main value of this textbook will be to stimulate others, new to theoretical rheology, to take it up as a serious study. An index, a bibliography, notes on some of the more mathematical points at the ends of chapters, and many diagrams, make this an easy book to read and to use for reference.

J. G. OLDROYD

Chemical Bonds

Coordination Chemistry. Edited by Arthur E. Martell. Vol. 1. Pp. xxii+577. (Van Nostrand Reinhold: New York and London, February 1972.) £16.25.

FROM a study of a group of transition metal compounds that did not seem to obey the inadequate theories of chemical bonding at the turn of the century, coordination chemistry has become an approach to inorganic chemistry that focuses attention upon bonding, stereochemistry, equilibrium and mechanism. This new series of three volumes seems to exhibit a desire to present the subject as it was in the glorious days of the late fifties and the early sixties and therefore suffers from all the consequences of trying to turn the clock back.

Volume 1 has apparently suffered an extremely long gestation period (one contribution was submitted in April 1967) and has been beset by unmet deadlines resulting in the need for some rearrangement in the series. It consists of two sections dealing with bonding and spectra and equilibrium and thermodynamics respectively. On the whole, the individual contributions are by distinguished and respected experts in their fields and are of a very high standard throughout. The first two chapters on electronic structures and electronic spectra are by Ballhausen and Gray and by McClure and Stephens respectively. Unfortunately, they overlap significantly at the edges because it should have been

obvious that the two subjects do not separate readily. Nakamoto writes on infrared spectra and shows that 50 pages are quite inadequate to cover the topic. He chooses to ignore the work of Hirashi that reassigns the C=C stretching frequency in olefin complexes. The treatment of electron spin resonance by Kuska and Rogers is excellent and Good and Clausen show that, at the moment, if one is interested in the chemistry of iron and tin, it is possible to gain considerable information from Mössbauer spectroscopy whereas devotees of other elements may have to wait patiently for a little longer. Holm and Abbott write on the application of nuclear magnetic resonance to the investigation of structure and bonding and have also included discussion on dynamic ligand exchange processes.

The second part of the book is opened by Hindman and Sullivan on principles and methods: they provide a useful treatment of solvation and solvation number. The examples of complex formation that follow are highly selective and serve to show that the simplified approach that once served to make the study of stability constants highly fashionable is of little value in its own right. Anderegg writes on complexation by multidentate ligands but throws no new light on the chelate effect; and Lars Gunnar Sillen, whose tragic death has robbed this area of chemistry of its leading proponent, contributes a posthumous article on polynuclear complexes in solution.

M. L. TOBE

Mouse Neuroanatomy

Atlas of the Mouse Brain and Spinal Cord. Edited by Richard L. Sidman, Jay B. Angevine jun. and Elizabeth Taber Pierce. Pp. xi+261. (Harvard University: Cambridge, Massachusetts; Oxford University: London, January 1972.) £12.

THIS is in fact an atlas of the central nervous system of the mouse strain C57BL/6J, chosen by the authors because of its interest to those concerned with the genetics of abnormalities in the central nervous system. It presents a large and comprehensive series of low power photomicrographs of the brain sectioned in all three planes, together with a series of cross sections of the spinal cord at all segmental levels. Additional diagrams of the gross external structure of the brain are provided with keys to enable the approximate position of each section to be determined relative to external features. There is little doubt that the nomenclature used in some regions will cause much blenching among specialists—as

much by omission as supposed "error"—but the system chosen can be defended at very least on the grounds that so little work has been carried out on the mouse brain that it is better to err on the side of neutrality than over-confident committal. Taken as a whole the book provides an excellent base-line for those who have no special interest in neuroanatomy *per se*, and as such it can be thoroughly recommended.

K. E. WEBSTER

Senescence

Principles of Mammalian Aging. By Robert R. Kohn. Pp. xiii+171. (Prentice Hall: Englewood Cliffs, New Jersey, October 1971.) \$7.95 cloth; \$4.95 paper.

MANY people in the field of gerontology will admit to having got there more or less accidentally. The reasons why biologists of any description should become interested in ageing are too numerous and mostly too obvious to mention. In this book the author sets out to map the main features of the field and thus make easier the tiro's first explorations. He succeeds well, providing a lucid factual account of the phenomena of ageing and outlining numerous areas of doubt and contention. Although the book is especially concerned with mammalian systems, the first two-thirds of it deal with the generalities of ageing at molecular and cellular levels, the relevance of which is by no means confined to the mammals.

Much is known about the ageing processes, but little is yet understood. Several groups of factors seem to contribute to ageing in mammals. Of these Kohn seems inclined to favour for the principal role those which are associated with changes in collagen, and he does perhaps a little less than full justice to possible cellular mechanisms. This may be partly because the literature since 1968 is not covered, and hence no account is taken of recent data which confirm the relationship between the limited life-span of human fibroblast strains *in vitro* and the ageing of cells *in vivo*. Similarly, neither Orgel's "error catastrophe" hypothesis nor the recent experimental work related to it is mentioned.

The dust-jacket states that "non-biologically oriented readers will find the answers to the questions about aging that plague everyone". They will not, and it seems most unlikely that the author himself would make any such claim. But the book will be a valuable introduction to the subject for many students of biology and medicine.

H. S. MICKLEM

CORRESPONDENCE

Science in India

SIR,—In your comments on Dr V. H. Shah's suicide in Delhi and the running of research councils (*Nature*, **237**, 131; 1972) you have rightly pointed out two significant factors in the maladministration of scientific institutions in India: direct control by the ministers, and undue domination of younger scientists by senior colleagues. However, these are not all, and possibly not even the major ones. I believe most of the scientists who return to India, sometimes with very productive careers abroad, would be quite satisfied to work in India, monetary hardships notwithstanding, if they had access to equipment, literature, computational aids and the possibility of scientific exchange and travel and just appraisal for advancement. The major obstacles here are not the senior colleagues or the ministers, but the civil services and kindred administrators and excessive administrative procedures, necessary in principle but which make the scarcity in all above aspects, otherwise natural in India, grave indeed. Science having been rendered virtually impossible and its habits and temper forgotten, scientists turn to "regionalism", "linguism" and considerations of personal contacts at the time of personnel selection, committee appointments, facility allocation, and so on. They do this for the sake of their own survival and advancement. Justice and objectivity in decision-making are not easy under such conditions.

I am, however, puzzled by your support for the denial of an enquiry. Democracy is government by voice. One cannot take one and discard the other. The administration of science is already "politicalized"; why then should not Parliament or other suitable body enquire when things are wrong? Surely, there should be room in a democracy to evaluate failures and suggest improvements. Dr Swaminathan's application of some methods successful elsewhere has nothing to do with the questions involved.

Lastly, I knew Dr Shah personally and I regarded him as one of the most promising Indian scientists in India. This sacrifice, as he possibly meant it to be, should not go in vain and scientists hope and expect that the new leadership will ensure a fair deal to science.

Yours faithfully,

R. K. MISHRA

Akron,
Ohio

Seismology

SIR,—This is in response to the letter from G. Ranalli (*Nature*, **236**, 413; 1972). Readers might have concluded from the wording of Dr Ranalli's letter that in our work on steep-incidence reflexions from the Earth's inner core (*Nature*, **228**, 852; 1970) we were unaware of the earlier observations pub-

lished by Caloi (*Geophys. J. Roy. Astron. Soc.*, **4**, 139; 1961). This was not the case. We made explicit reference to Caloi's work both in our published paper and in the oral presentation before the Seismological Society of America.

Many seismologists have been sceptical of Caloi's identifications of PKiKP, especially since subsequent theoretical calculations by Bolt and O'Neill (*Geophys. J. Roy. Astron. Soc.*, **9**, 223; 1965) showed that the phase in question should be well below the level of detectability in normal observational circumstances. In our work we were fortunate to have available the Large Aperture Seismic Array in Montana, and found that it required the full beam-forming capability of this array to bring PKiKP up out of the noise and identify it with confidence. Additionally, we were able to measure directly the apparent surface velocity of the phase across the large array, verifying that it was PKiKP, and not just a random noise pulse at the predicted time.

Yours faithfully,

E. R. ENGBAHL

National Ocean Survey,
Boulder, Colorado

E. A. FLINN

Teledyne Geotech,
Alexandria, Virginia

C. F. ROMNEY

Vela Seismological Center,
Alexandria, Virginia

Obituary

Arthur Wilson Stelfox



ARTHUR WILSON STELFOX, ALS, MRJA, died on May 19 at the age of 88.

In 1920 he abandoned his profession as an architect to devote all his time to natural history joining the staff of the National Museum in Dublin and working there until his retirement in 1948. In 1956 he moved to Newcastle, Co Down, bringing with him the wonderful collection of plants that had made his garden in Harolds Cross so interesting, and at the age of 73 commenced to create from a rough field the garden that became a research plot, a refuge for rare plants and a delight to the eye. In it could be found plants which are now extinct in their wild habitats in Britain and Ireland. The native plant beds at the Botanic Gardens, Glasnevin, contain many important specimens from his collection and his friends also were generously supplied.

He was interested in botany from childhood and for many years was the recognized authority on plant distribution in Ireland. While a young man he became a European authority on land and freshwater snails, particularly in distributional problems. He embarked on experimental genetics with the descendants of a pair of snails found in his garden in Harolds Cross and by selective breeding produced a variant of such interest to geneticists that his "line" of snails is now being bred in both hemispheres.

In 1920 he started to study Hymenoptera—the bees, wasps and ants—and from them he progressed to the minute parasitic Hymenoptera, restoring to order the pioneer collection of A. H. Haliday which had been reduced to chaos about a century earlier, and finally deciphering much of the "shorthand"

in which Haliday's notes were written.

In 1967 he presented to the Smithsonian Institution, Washington, his vast collection of 90,000 beautifully mounted insects because no other museum had so many specialists in the subject. The types of the many species new to science described by him are in this collection.

In the early 1900s he was one of the dedicated group who raised the status of the Irish Field Clubs to their highest level. He was editor of the *Irish Naturalist* for years and an adviser and copious contributor to the *Irish Naturalists' Journal* until his death.

He studied the skeletons of birds and small animals found in cave deposits and became so proficient he could identify most species of birds from only two bones. His knowledge of surface geology made any drive with him memorable.

Together with his wife who was also a botanist, he kept open house wherever he resided and especially welcomed the younger generation. His dedication to natural history left no time for public or social engagements but its benefit to present and future naturalists is inestimable.

[Reprinted from the *Irish Times*

Professor Harusada Suginome



HARUSADA SUGINOME, Chairman of the Japanese National Commission for UNESCO, died on April 14, 1972, in Sapporo, Japan, aged 79. With his death Japan has lost not only a distinguished organic chemist but also a staunch worker in the cause of international scientific cooperation.

Born in Sendai, the old traditional city in the north-eastern district of the Japanese mainland, Suginome graduated from Tohoku University to work with the late Professor Rikoh Majima on the chemistry of aconite alkaloids, a group of very toxic substances. In 1925 he was

the first Japanese recipient of a Rockefeller scholarship for studying abroad, and he became a collaborator of Sir Robert Robinson's in the Department of Organic Chemistry at the University of Manchester, where he remained until 1927. His research in Manchester was concerned with indolenine in connexion with the synthesis of physostigmine (eserine). During his stay in England he became an ardent anglophile and a life member of the London Chemical Society.

After his return to Japan in 1928 he became Professor of Organic Chemistry in the newly created Faculty of Science, Hokkaido University, at Sapporo in 1930. He continued his fundamental studies of aconite alkaloids, which were a poorly understood group of complex natural products at that time, and initiated work on veratrum alkaloids and carotenoids although the great shortage of equipment and chemicals during and immediately after the Second World War created severe difficulties for his research. In spite of this Suginome was nevertheless able to make significant contributions to the isolation and structural elucidation of aconite alkaloids. For this distinguished work, he received the Hattori Hohkokai Prize (1950) and the award of the Chemical Society of Japan (1951), of which he became president in 1967. In 1954, after four fruitful years as Dean of the Faculty of Science, he was elected President of Hokkaido University, a position he held until 1966. During this period he devoted much of his attention to educational affairs and expansion of the university.

Suginome also took an active part in public affairs and he regarded it as his duty to contribute to the development of Hokkaido, serving as President of the Hokkaido District Government Council for Science and Technology and as Chairman of the Committee for Development of Hokkaido as well as on other committees associated with the district government. As a firm believer that the public should be properly informed on scientific matters, he was chosen to be a member of the Managing Committee of the Japan Broadcasting Corporation (NHK), and from 1966 until his death he served on the Council for Science and Technology of Japan.

But it was in the field of international cooperation that Suginome's chief contribution was made in his later years. He visited the United Kingdom, the United States and many other countries, often as chairman of delegations, promoting the cause of international scientific understanding, and in 1961 he was selected as a member of the Japan-United States Committee on Scientific Cooperation. In 1966 he became the first president of the British-Japanese Society in Hokkaido and the Japanese

representative to the Japan-United States Committee on Cultural and Educational Cooperation. In 1971 he became the first president of the UNESCO Asian Cultural Centre.

In recognition of his many achievements, His Majesty the Emperor conferred on him the First Class of the Order of the Sacred Treasure in 1967.

A gentle unassuming man, Suginome nevertheless stood firm by ideas and ideals in which he believed. International science will be the poorer for his death.

Announcements

International Meetings

August 2-4, **Applications of X-ray Analysis**, Denver (Dr C. O. Ruud, Metallurgy and Materials Sciences Division, Denver Research Institute, University of Denver, Colorado 80210, USA).

August 7-11, **Atomic Physics**, Boulder (S. J. Smith, Joint Institute for Laboratory Astrophysics, University of Colorado, Boulder, Colorado 80302, USA).

August 7-14, **Biophysics**, Moscow (Secretary-General, Fourth International Biophysics Congress, Profsoyuznaya 7, Moscow V-133, USSR).

August 9-11, **Reindeer/Caribou**, Fairbanks, Alaska (R. G. White, Institute of Arctic Biology, University of Alaska, Fairbanks, Alaska 99701, USA).

August 13-17, **Biology of the Seal**, Guelph (Professor K. Ronald, College of Biological Sciences, University of Guelph, Guelph, Canada).

August 14-18, **Physics and Chemistry of Ice**, Ottawa (M. K. Ward, National Research Council of Canada, Montreal Road, Ottawa 7, Canada).

August 14-18, **Numerical Analysis**, Dublin (Dr J. Miller, School of Mathematics, Trinity College, Dublin 2, Ireland).

August 14-18, **ANZAAS Congress**, Sydney (ANZAAS Congress Executive Officer, University of New South Wales, PO Box 1, Kensington, NSW, Australia).

August 14-18, **Cosmochemistry**, Cambridge, Massachusetts (Professor A. G. W. Cameron, Belfer Graduate School of Science, Yeshiva University, Amsterdam Avenue and 186th Street, New York, NY 10033, USA).

August 15-18, **International Primatological Society Congress**, Portland, Oregon (Dr William Montagna, ORPRC, 505 NW 185th Avenue, Beaverton, Oregon 97005, USA).

August 16-19, **Strontium Metabolism**, Glasgow (Dr J. M. A. Lenihan, Department of Clinical Physics and Bioengineering, Western Regional Hospital Board, 11 West Graham Street, Glasgow G4 9LF).

August 20–25, **Combustion**, University Park, Pennsylvania (Conference Center, J. Orvis Keller Building, University Park, Pennsylvania 16802, USA).

August 21–22, **Control of Mycotoxins**, Kungälv, near Gothenburg (Secretariat of the Symposium on Mycotoxins, c/o SIK, Fack, S-400 21 Göteborg 16, Sweden).

August 21–25, **Sport in the Modern World: Chances and Problems**, Munich (Organisationskomitee für die Spiele der XX Olympiade München 1972, 8000 München 13, Saarstrasse 7, Germany).

August 21–25, **Hydrogen Bonding**, Ottawa (M. K. Ward, National Research Council of Canada, Ottawa K1A 0R6, Canada).

August 21–25, **Underwater Physiology**, Freeport, Bahamas (Dr C. J. Lambertsen, Institute for Environmental Medicine, University of Pennsylvania, 36th Street and Hamilton Walk, Philadelphia, Pennsylvania 19104, USA).

August 21–25, **Liquid Crystals**, Kent, Ohio (Dr Glenn H. Brown, Liquid Crystal Institute, Kent State University, Kent, Ohio 44242, USA).

August 21–30, **International Geological Congress**, Montreal (Secretary-General, 24th International Geological Congress, 601 Booth Street, Ottawa 4, Canada).

August 22–30, **Entomology**, Canberra (The Secretary, 14th International Congress of Entomology, The Australian Museum, College Street, Sydney, Australia 2000).

August 28–September 2, **Antibiotics: Biosynthesis and Function**, Aarhus (Professor J. Hedegaard, Department of Microbiology, The Polytechnical University, DK 2800 Lyngby, Copenhagen, Denmark).

Reports and Publications

not included in the Monthly Books Supplement
Great Britain and Ireland

The Annual Report of the Committee of Visitors of the Royal Institution of Great Britain; The Statement of Accounts and Other Reports for the year ending 31 December 1971. Pp. 64. (London: The Royal Institution, 1972.) [155]

University of Oxford. Ashmolean Museum—Report of the Visitors 1972. Pp. 69. (Oxford: The University, 1972.) £1. [155]

Rowett Research Institute. Annual Report of Studies in Animal Nutrition and Allied Sciences, Vol. 27, 1971. Pp. 122. (Bucksburn, Aberdeen: Rowett Research Institute, 1972.) 70p; \$1.70. [155]

Cotton Research Corporation. Progress Reports from Experiment Stations, Season 1969–70. Republic of the Sudan. Pp. 48. 30p. Zambia. Pp. 38. 30p. (London: Cotton Research Corporation, 1971 and 1972.) [155]

University of Leeds. The Brotherton Library—Annual Report of the Librarian, Session 1970–71. Pp. 16. (Leeds: The University, The Brotherton Library, 1972.) [155]

Proceedings of the Royal Irish Academy. Vol. 72, Section A, No. 6: On Operators T Such That $f(T)$ is Riesz or Meromorphic. By M. A. Kaashoek and M. R. F. Smyth. Pp. 31–88. (Dublin: Royal Irish Academy, 1972.) 14p. [155]

The University of Sussex. Science Policy Research Unit—Annual Report for 1971. Pp. 56. (Falmer, Brighton: SPRU, The University of Sussex, 1972.) [155]

Department of Education and Science. Growing Points in Science. Pp. v+215+20 plates. (London: HMSO, 1972.) 60p net. [165]

The Institution of Gas Engineers. Communications. No. 868: Natural Gas as a Factor in Air

Pollution Control. By Dr. Alice Garnett and P. Read. Pp. 23. 75p. No. 869: The International Consultancy Service—an Economic and Social Force in Global Gas Industry. By C. E. Mills. Pp. 16. 75p. No. 871: Experience Gained in the Commissioning of the LNG Storage Installation in Stuttgart. By Dr. Heinz Berge and Jürgen Poll. Pp. 9. 75p. No. 872: Long Distance Liquid Natural Gas Pipelines. By Prof. G. Walker, Prof. D. M. Coulter and Prof. D. H. Norrie. Pp. 19. 75p. No. 873: Some Design Considerations and Operational Experience with UK Gas Compressor Stations. By A. Cleveland and D. A. Young. Pp. 31. 75p. No. 874: Converting Customer Service. By B. C. Smith and H. B. Healy. Pp. 22. 75p. No. 875: Marketing—Southern Style. By J. F. Doran. Pp. 29. 75p. No. 876: Gas Control with an On-Line Computer. By K. R. Brookes and A. W. Coles. Pp. 26. 75p. No. 877: Change and Exchange in International Energy Supply. By Carrol V. Kroeger. Pp. 24. 75p. (London: The Institution of Gas Engineers, 1972.) [175]

Building Research Station Current Paper 9/72: Slab Design—Past, Present and Future. By R. H. Wood. (Reprinted from ACI Publication SP-30.) Pp. 16. (Garston, Watford: Building Research Station, 1972.) gratis. [175]

West of Scotland Agricultural College: Advisory and Development Division. Publication No. 320: Classification of Herbage Plant Varieties for West of Scotland Conditions 1972. By L. V. Hunt, F. Frame and R. D. Harkness. Pp. 37. (Auchincruive, Ayr: West of Scotland Agricultural College, 1972.) [185]

The Kent Incorporated Society for Promoting Experiments in Horticulture. East Malling Research Station—Report for 1971, 1st October 1970 to 30th September 1971. Pp. xii+190. (East Malling, Maidstone: East Malling Research 1972.) £1.25. \$4.60. [185]

Report to the Worshipful Company of Clothworkers of the City of London of the Advisory Committee on the Departments of Textile Industries and Colour Chemistry and Dyeing in the University of Leeds for the Session 1970–71. Pp. 75. (Leeds: The University, 1972.) [195]

University of Oxford. Report of the Committee on Entitlement. Pp. 13. (Supplement No. 5 to the *University Gazette*, May 1972.) (Oxford: The University, 1972.) 50p. [195]

Computation and Communication. By Professor Glyn Emery (An Inaugural Lecture delivered at the University College of Wales, Aberystwyth, on 13 October 1971.) 25p. [195]

Institution of Gas Engineers. Communication No. 867: Presidential Address by J. A. Buckley. Pp. 17. 75p. (109th Annual General Meeting, London, 16th, 17th and 18th May, 1972.) Communication No. 870: The Glenmavis Natural Gas Liquefaction and Storage Facility—Experiences in its Design, Construction and Commissioning. By A. B. Garbutt, Dr. E. B. Graham and L. Thompson. Pp. 35. 75p. (London: The Institution of Gas Engineers, 1972.) [195]

The Commonwealth Forestry Institute, University of Oxford. Forty-seventh Annual Report, 1970/1971. Pp. 26. (Oxford: Commonwealth Forestry Institute, 1972.) [225]

Research and Teaching. By Professor L. R. B. Elton. (Inaugural Lecture delivered at the University of Surrey, 10 November 1971.) Pp. 12. (Guildford, Surrey: University of Surrey, 1971.) [225]

Institution of Mechanical Engineers. Annual Report of the Council for the year 1971. Pp. 221–267. (London: Institution of Mechanical Engineers, 1972.) [235]

Conversion to Natural Gas: a Guide for Industry. Pp. 16. (London: The Gas Council, 1972.) [245]

University of Oxford. Report of the Committee on Co-residence. Pp. 12. (Supplement No. 6 to the *University Gazette*, May 1972.) (Oxford: The University, 1972.) 50p. [255]

Ministry of Agriculture, Fisheries and Food. Fishery Investigations, Series II, Volume 27, No. 1: Simulation of the Changes in Abundance of the Cod (*Gadus morhua* L.) and the Distribution of Fishing in the North Atlantic. By A. D. Clayden. Pp. vii+58. (London: HMSO, 1972.) £1.50 net. [255]

British Flame Research Committee. 1971 Annual Report. (16th Annual General Meeting, 3rd May 1972.) Pp. 26. (London: British Flame Research Committee, 1972.) [255]

Young Fabian Pamphlet No. 30: British Entry—Labour's Nemesis. By James Bellini. (Into the Seventies.) Pp. 24. (London: Fabian Society, 1972.) 25p. [265]

British Geological Literature. New Series. Vol. 172, Part 1. Compiled by Brown's Geological Information Service, Ltd., London. Edited by Nicholas Edwards. Pp. ii+32. Published quarterly. Subscription: £4 per annum in UK and Europe; £5 by airmail to other countries. (Worthing: Dr. N. Edwards, British Geological Literature, 10 Montague Place, 1972.) [265]

Natural Environment Research Council. Monks Wood Experimental Station—Report for 1969–1971. Pp. 118. (Abbots Ripton, Huntingdon: The Nature Conservancy, Monks Wood Experimental Station, 1972.) 60p net. [265]

Freshwater Biological Association. Scientific Publication No. 15: A Revised Key to the Adults of the British Species of Ephemeroptera with Notes on their Ecology. By D. E. Kimmins. Second revised edition. Pp. 75. (Ambleside, Westmorland: Freshwater Biological Association, 1972.) 60p. [305]

Building Research Station Digest, No. 142: Fill and Hardcore. Pp. 4. (London: HMSO, 1972.) 5p. [305]

Philosophical Transactions of the Royal Society

of London. B: Biological Sciences. Vol. 264, No. 859: The Secretion and Structure of the Skeleton of Living and Fossil Bryozoa. By R. Tavener-Smith and A. Williams. Pp. 97–159+plates 6–30. (London: The Royal Society, 1972.) £3.65; \$10.20. [305]

The Filter-Well Technique for Studying the Biochemistry of Cell Populations. By J. A. Dickson. Pp. 31. An Introduction to the Use of Tetrazolium Salts in Quantitative Enzyme Cytochemistry. By F. P. Altman. Pp. 45. (Colnbrook, Bucks: Koch-Light Laboratories, Ltd., 1972.) [305]

Research Using Transplanted Tumours of Laboratory Animals: a Cross-Referenced Bibliography—VIII. By D. C. Roberts. Pp. 161. (Mill Hill, London: Registry and Information Service for Experimental Tumours, Research Data Unit, Imperial Cancer Research Fund, 1972.) [16]

EMI Underwater Technology. Pp. 8. (Hayes, Middx.: EMI Limited, 1972.) [16]

Home-Grown Cereals Authority. Progress Reports on Research and Development, 1971/1972. Pp. 43. (London: Home-Grown Cereals Authority, 1972.) [16]

Department of the Environment. Welsh Office. Area Improvement Note 4: House Improvement and Conversion. Pp. 52. 65p net. Area Improvement Note 5: Environmental Design in Four General Improvement Areas. Pp. 21. 55p net. (London: HMSO, 1972.) [16]

Office of Population Censuses and Surveys—Social Survey Division. The Youth Service and similar provision for Young People. By Margaret Bone, assisted by Elizabeth Ross. (An enquiry carried out on behalf of the Department of Education and Science.) Pp. xviii+292. (London: HMSO, 1972.) £3 net. [16]

From Birth to Seven: The Second Report of the National Child Development Study (1958 Cohort). By Ronald Davie, Neville Butler, Harvey Goldstein, with the assistance of Eva Alberman, E. Ross and Peter Wedge. (Studies in Child Development.) Pp. xvii+198. (London: Longman Group Limited, in association with The National Children's Bureau, 1972.) £2 net. [16]

Other Countries

The Work of the World Health Organization in 1971: Annual Report of the Director-General. Pp. xvii+401. (Geneva: WHO; London: HMSO, 1972.) 15 Sw. francs, £1.50, \$3.75. [214]

Annals of the South African Museum. Vol. 59, Part 3: Larval Development of Three Species of Economically Important South African Fishes. By E. H. Haigh. Pp. 47–70. R.2.20. Vol. 59, Part 4: A Pliocene Phocid from South Africa. By Q. B. Hendey and C. A. Repenning. Pp. 71–98+plates 2–18. R.4.00. Vol. 59, Part 5: The Evolution and Dispersal of the Monachinae (Mammalia: Pinnipedia). By Q. B. Hendey. Pp. 99–113. R.1.40. Vol. 59, Part 6: A Pliocene Ursid from South Africa. By Q. B. Hendey. Pp. 115–132+2 plates. R.2.00. (Cape Town: South African Museum, 1972.) [214]

Journal of Psycholinguistic Research, Vol. 1, No. 1, 1971. Published quarterly. Pp. 1–126. Subscription rates: Volume 1, 1971 (4 issues), \$28. Price for individual subscribers certifying that the journal is for their personal use only, \$18. Outside USA and Canada add \$1.80 for postage and handling. (New York and London: Plenum Press, 1971.) [244]

United States Naval Observatory. Circular No. 136: Observations of the Sun, Moon, and Planets—Six-inch Transit Circle Results. By B. L. Klock and D. K. Scott. Pp. 20. Circular No. 137: Ephemeris of the Radio Longitude of the Central Meridian of Jupiter, System III (1957.0). By B. L. Morrison and Victoria Meiller. Pp. 4. (Washington, DC: United States Naval Observatory, 1972.) [244]

CERN. Very Elementary Theory of Weak Interactions. By J. S. Bell. (Lecture given in the Academic Training Programme of CERN, 1971–1972.) Pp. 28. (Geneva: CERN, 1972.) [244]

US Geological Survey. Professional Paper 640–E: Cheilostome Bryozoa of Late Eocene Age from Eua, Tonga. By Alan H. Cheetham. Pp. vi+26+7 plates. (Washington, DC: Government Printing Office, 1972.) 70 cents. [244]

World Health Organization. Biological Substances: International Standards, Reference Preparations, and Reference Reagents 1972. Pp. 56. (Geneva: WHO; London: HMSO, 1972.) 4 Sw. francs; 40p; \$1. [254]

Smithsonian Contributions to Botany. No. 5: The Woods and Flora of Florida Keys 'Pinnatae'. By Barrett Nelson Rock. Pp. 35. 50 cents. Smithsonian Contributions to Paleobiology. No. 11: Homeomorphy in Recent Deep-Sea Brachiopods. By G. Arthur Cooper. Pp. iii+25 (3 plates). 50 cents. Smithsonian Contributions to Zoology. No. 98: The Shrimps of the Smithsonian-Bredin Caribbean Expeditions with a Summary of the West Indian Shallow-water Species (Crustacea: Decapoda: Natantia). By F. A. Chace, Jr. Pp. x+179. \$2. [244]

No. 102: Systematics and Zoogeography of the Genus *Synidotea* (Crustacea: Isopoda) with an Account of Californian Species. By Robert J. Menzies and Milton A. Miller. Pp. 33. 45 cents. No. 105: Origins and Affinities of the Troglitic Crayfishes of North America (Decapoda: Astacidae). II. Genus *Orconastes*. By Horton H. Hobbs, Jr., and Thomas C. Barr, Jr. Pp. iii+84. \$1.25. No. 108: A Review of the Genus *Zopherus* of the World (Coleoptera: Tenebrionidae). By Charles A. Triplehorn. Pp. 24 (4 plates). 45 cents. No. 114: Parasitic Bees of the Genus *Holcopaspites* Ashmead (Hymenoptera: Apoidea). By Paul D. Hurd, Jr., and E. Gorton Linsley. Pp. 41. 50 cents. (Wash-

ington, DC: Smithsonian Institution Press, 1972. For sale by US Government Printing Office.) [254]

World Health Organization. Technical Report Series No. 492: The Medical Uses of Ionizing Radiation and Radioisotopes—Report of a Joint IAEA/WHO Expert Committee. Pp. 56. (Geneva: WHO London: HMSO, 1972.) 5 Sw. francs; 50p; \$1.25. [254]

East African Community. East African Virus Research Institute Report, 1970. (No. 20.) Pp. 1+88. (Entebbe, Uganda: East African Virus Research Institute, 1971.) Shs. 8. [254]

United States Department of the Interior: Geological Survey. Water-Supply Paper 1873-C: Physical, Chemical, and Biological Aspects of the Duwamish River Estuary, King County, Washington, 1963-67. By J. F. Santos and J. D. Stoner. Pp. vi+74. 40 cents. Water-Supply Paper 1968: The Hydrology of Four Streams in Western Washington as Related to Several Pacific Salmon Species. By M. R. Collings, Ronald W. Smith and G. T. Higgins. Pp. viii+109. 55 cents. Water-Supply Paper 1982: Chemical Quality of Water in the Walnut River Basin, South-Central Kansas. By Robert B. Leonard. Pp. viii+113+3 plates. Water-Supply Paper 1988: Definition of Selected Ground-Water Terms—Revisions and Conceptual Refinements. By S. W. Lohman. Pp. vi+21. 25 cents. Water-Supply Paper 1999-D: Underground Storage of Imported Water in the San Geronio Pass Area, Southern California. By R. M. Bloyd, Jr. Pp. iv+37. \$1. Professional Paper 605-B: Seismic Refraction Survey of Pleistocene Drainage Channels in the Lower Great Miami River Valley, Ohio. By Joel S. Watkins and Andrew M. Spicker. Pp. iii+17+1 plate. \$1.25. (Washington, DC: Government Printing Office, 1971 and 1972.) [254]

International Cooperation for Pollution Control. (UNITAR Research Report No. 9.) By Daniel Serwer. Pp. iii+73. (New York: United Nations Institute for Training and Research, 1972.) \$2.50. [264]

World Health Organization. Technical Report Series. No. 486: WHO Expert Committee on Biological Standardization—Twenty-fourth Report. Pp. 63. 5 Sw. francs; 50p; \$1.25. No. 489: Implications of Individual and Small Group Learning Systems in Medical Education—Report of a WHO Study Group. Pp. 29. 4 Sw. francs; 40p; \$1. No. 492: The Medical Uses of Ionizing Radiation and Radioisotopes—Report of a Joint IAEA/WHO Expert Committee. Pp. 56. 5 Sw. francs; 50p; \$1.25. (Geneva: WHO; London: HMSO, 1972.) [264]

World Health Organization. International Non-proprietary Names for Pharmaceutical Substances—Cumulative List No. 3. Pp. 189. (Geneva: WHO; London: HMSO, 1971.) 24 Sw. francs; £2.40; \$6. [264]

First Malaysia Plan Land Capability Classification Report, West Malaysia. By P. C. Lee and W. P. Pantan. (Economic Planning Unit, Prime Minister's Department, Malaysia.) Pp. vi+64+5 maps. (Kuala Lumpur: Bahagian Perancangan Ekonomi, Jabatan Perdana Menteri, 1971.) [264]

US Department of the Interior: Geological Survey. Professional Paper 727: Distribution of Gold in Igneous Rocks. By David Gottfried, Jack J. Rowe and Robert I. Tilling. Pp. iv+42. 50 cents. Professional Paper 750: Geological Survey Research 1971. Pp. viii+418. \$3.25. (Washington, DC: Government Printing Office, 1971 and 1972.) [264]

The Application of Physics to Industry. (A series of lecture-discussions held at The University of New South Wales, September-October, 1971.) Edited by J. S. Blakemore and C. J. Milner. Pp. 106. (Kensington, NSW: Department of Applied Physics, The University of New South Wales, 1972.) \$3. [264]

US Department of the Interior: Geological Survey. Bulletin 1353-B: Mineral Resources of the Popo Agie Primitive Area, Fremont and Sublette Counties, Wyoming. By Robert C. Pearson, Thor H. Killsgaard and Lowell L. Patten. With a section

on Interpretation of Aeromagnetic Data by Robert E. Mattick. Pp. vi+55. (Washington, DC: Government Printing Office, 1971.) [264]

Fisheries Research Board of Canada. Technical Report No. 310: DUCCS—a Collapsible Underwater Camera Sled for Sea-Bed Photography from a Drifting Support Vessel. By T. J. Foulkes and J. F. Caddy. Pp. 8. (St. Andrews, NB: Fisheries Research Board of Canada, 1972.) [284]

Smithsonian Contributions to Zoology. No. 115: Bredin-Archbold-Smithsonian Biological Survey of Dominica—Aculeate Wasps (Hymenoptera: Scolioidea, Vespidae, Pompilidae, Sphecidae). By Howard E. Evans. Pp. 19. 35 cents. No. 117: The Subgenera of the Crayfish *Procambarus* (Decapoda: Astacidae). By Horton H. Hobbs, Jr. Pp. 22. 35 cents. No. 118: Studies of Neotropical Caddisflies, XIII: The Genus *Ochrotrichia* from Mexico and Central America (Trichoptera: Hydropsychidae). By Oliver S. Flint, Jr. Pp. 28. 40 cents. (Washington, DC: Smithsonian Institution Press, 1972. For sale by US Government Printing Office.) [284]

Archives of Sexual Behavior. Vol. 1, No. 1, 1971. Pp. 1-102. Published quarterly. Subscription rates: Vol. 1, 1971 (4 issues), \$26. Price for individual subscribers certifying that the journal is for their personal use \$16. Outside the US and Canada add \$1.80 for postage and handling. (New York and London: Plenum Press, 1971.) [15]

Population Bulletin. Vol. 28, No. 1, February 1972: Suburban Growth—a Case Study. Pp. 30. (Washington, DC: Population Reference Bureau, Inc., 1972.) [15]

Unesco. Status and Trends of Research in Hydrology, 1965-74/Bilan et Tendances de la Recherche en Hydrologie, 1965-74. (A contribution to the International Hydrological Decade.) Pp. 148. (Paris: Unesco; London: HMSO, 1972.) 24 francs; £1.80; \$6. [15]

National Geophysical Research Institute, Hyderabad. Annual Report for 1970/1971. Pp. iii+97. (Hyderabad: National Geophysical Research Institute, CSIR, 1971.) [15]

Comptes Rendus des Séances de la Quatorzième Conférence Générale des Poids et Mesures, Paris, 4-8 Octobre 1971. Pp. 142. (Sèvres, France: Bureau International des Poids et Mesures, 1972.) [15]

Bulletin of the American Museum of Natural History. Vol. 147, Article 5: The Systematics of the North American Family Baenidae (Reptilia, Cryptodira). By Eugene S. Gaffney. Pp. 241-320. (New York: American Museum of Natural History, 1972.) \$3.95. [25]

Institut Royal Météorologique de Belgique. Publications Série B, No. 65: Etude Statistique des Inversions dans la Structure Thermique Verticale de l'Atmosphère à Uccle. Par A. G. Maenhout et M. Legrand. Pp. 12. (Uccle-Bruxelles: Institut Royal Météorologique de Belgique, 1972.) [25]

US Atomic Energy Commission. Annual Report to Congress of the Atomic Energy Commission for 1971. Pp. xi+249. Fundamental Nuclear Energy Research 1971. (A Supplemental Report to the Annual Report to Congress for 1971 of the US Atomic Energy Commission.) Pp. xvi+159. \$1.50. (Washington, DC: Government Printing Office, 1972.) [25]

Smithsonian Contributions to Zoology. No. 114: Parasitic Bees of the Genus *Holcopasites* Ashmead (Hymenoptera: Apoidea). By Paul D. Hurd, Jr., and E. Gorton Linsley. Pp. 41. (Washington, DC: Smithsonian Institution Press, 1972. For sale by US Government Printing Office.) 50 cents. [25]

US Department of the Interior: Geological Survey. Bulletin 1335: Sedimentary and Igneous Rocks of the Grays River Quadrangle, Washington. By Edward W. Wolfe and Edwin H. McKee. Pp. v+70. 40 cents. Professional Paper 693: Field Instrumentation Studies of Earth Tremors and Their Geologic Environments in Central Utah Coal Mining Areas. By Frank W. Osterwald, John B. Bennett,

Jr., C. Richard Dunrud and John O. Maberry. Pp. iii+20. 35 cents. (Washington, DC: Government Printing Office, 1971 and 1972.) [25]

Consiglio Nazionale delle Ricerche, Roma. Quaderni de La Ricerca Scientifica, Nr. 74: Libro Bianco sulla Natura in Italia. A cura di L. Contoli and S. Palladino. (Commissione di Studio per la Conservazione della Natura e delle Sue Risorse. Pp. 418. Programma di Ricerca Territoriale sulle Aree Naturali da Proteggere. 1: Carta dei Biotopi d'Italia. Pp. 268. 2: Carte Regionali dei Biotopi, Lazio. Pp. 41. (Roma: Consiglio Nazionale delle Ricerche, 1971.) [35]

British Columbia Research. 28th Annual Report, 1971. Pp. 20. (Vancouver: BC Research, 1972.) [45]

The Life Insurance Medical Research Fund of Australia and New Zealand: The First 20 Years. Pp. ix+69. (Sydney: The Life Offices' Association of Australia and New Zealand, 1971.) [45]

Biologische Bundesanstalt für Land- und Forstwirtschaft, Berlin-Dahlem. Bibliographie der Pflanzenschutz-Literatur/Bibliography of Plant Protection. Neue Folge, Band 7, Heft 1. Nearbeit von Dr. W. Laux, unter Mitarbeit von Dr. W. Sicker und Dr. D. Blumenbach. Pp. 159. (Berlin-Dahlem: Biologische Bundesanstalt für Land- und Forstwirtschaft, 1972.) 20 DM. [45]

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